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A STUDY OF THE TEETH OF A GROUP OF SCHOOL CHILDREN PREVIOUSLY EXAMINED FOR RICKETS

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The problem of the relation of rickets to defective formation of teeth and to the occurrence of dental caries is one that has been of increasing interest to investigators in recent years, and one regarding which various and differing opinions have been expressed as a result of clinical investigations and animal experimentation. The data reported in the present study are entirely clinical and have to do with observations on the permanent teeth of children whose previous history with regard to rickets is known. A review of recent literature shows that few clinical investigations have been undertaken that deal with the relation of rickets to defects of the teeth, either defects of structural development or caries.

MacKay and Rose,[1] in 1931, reported a study of the incidence of dental defects in the permanent teeth of two groups of children; the first, a group of 46 who in infancy had shown evidences of rickets at clinical examination, and the second, a group of 40 who had shown no clinical evidence of the disease in early life. Though they found that hypoplasia of the permanent teeth occurred more frequently in the rachitic group, the amount of caries was only slightly greater in this group than in the control group. They concluded from their findings that "D deficiency in infancy and early childhood, with consequent hypoplasia of the permanent teeth, is not the main factor in determining the incidence of dental caries."

Hess and Abramson,[2] approaching the problem in a similar manner, studied the incidence of caries and of defects in the enamel in the

From the New Haven Rickets Studies of the United States Children's Bureau in collaboration with the Pediatric and Surgical Department of the Yale University School of Medicine.

1. MacKay, H. M. M., and Rose, S. F.: Vitamin D Deficiency, Dental Caries and Tonsillar Enlargement, Lancet **2**:1230, 1931.

2. Hess, A. F., and Abramson, H.: The Etiology of Dental Caries, Dental Cosmos **73**:849, 1931.

deciduous teeth of a group of children known to have had rickets in infancy and also the incidence of the same defects in a group of children who had been protected against rickets in infancy. They reported that "caries of the deciduous teeth occurred less often in the protected than in the rachitic group" and further stated that "lesions of the enamel were by no means confined to or associated with infantile rickets."

In 1922, Dick [3] reported examinations of the permanent teeth of 586 "rickety" children of school age and stated that "20 per cent of these showed hypoplasia frequently combined with decay" and that, in addition, 38 per cent had decayed teeth only.[3a] Though he did not compare this group of "rickety" children with a group of normal children nor give the basis for his diagnosis of rickets, his report is of some interest in connection with the present study. He pointed out, however, that "other (than syphilitic) forms of hypoplasia are exceedingly common, and probably affect some seven or eight per cent of the whole population." [3b] He also found hypoplasia to be much more common in a group of 281 children whose nutrition and environment were decidedly poor (40 per cent) than in a group living under good social conditions (13 per cent).[3c]

The Committee for the Investigation of Dental Diseases of the British Medical Research Council [4] reported, in 1925, a study of the incidence of hypoplasia and dental caries in a group of children largely of school age but did not state whether the children were known to have had rickets in early life. Of the total group of children studied, 11.5 per cent showed some form of hypoplasia of the permanent teeth.

Recently several clinical studies that have had to do primarily with the effect of diet on the prevention or arrest of dental caries have been reported, notably those by Boyd and Drain,[5] Bunting, Jay and Hard,[6] McBeath,[7] Hanke [8] and Jones [9] in this country and by Mellanby and

3. Dick, J. L.: Rickets, London, W. Heinemann, 1922, (*a*) p. 202; (*b*) p. 197; (*c*) p. 205.

4. Report of the Committee for the Investigation of Dental Diseases: II. The Incidence of Dental Disease in Children, Medical Research Council, Special Report Series, no 97, London, His Majesty's Stationery Office, 1925.

5. Boyd, J. D., and Drain, C. L.: The Arrest of Dental Caries in Childhood, J. A. M. A. **90**:1867 (June 9) 1928.

6. Bunting, R. W.; Jay, P., and Hard, D. G.: Observations in the Examination of the Mouths of 1192 Children in Public Schools and Institutions, J. Dent. Research **12**:444, 1932.

7. McBeath, E. C.: Experiments on the Dietary Control of Dental Caries in Children, J. Dent. Research **12**:723, 1932.

8. Hanke, M. T.: Diet as a Factor in Control of Gingivitis; and Diet as a Factor in Control of Dental Caries, J. Dent. Research **12**:518, 1932.

9. Jones, M. R.: Larsen, N. P., and Pritchard, A. P.: Dental Cosmos **72**: 439, 1930; Dental Disease in Hawaii, J. A. M. A. **99**:1849 (Nov. 26) 1932; Dental Disease in Hawaii, Am. J. Dis. Child. **45**:789 (April) 1933.

Pattison,[10] Sprawson[11] and investigators for the Committee upon Dental Disease of the Medical Research Council[12] in England. Although in several of the investigations special attention was paid to the inclusion of vitamin D in the diet given during the period of the study, it is striking that in none of them were data available to indicate whether or not the children had had rickets in early life or had been given antirachitic treatment in infancy.

In an attempt to show whether rickets or a rickets-producing diet has any direct effect on the production of dental caries much experimental work has been done, though with very conflicting results. For a discussion of dietary and other factors involved in the production of enamel hypoplasia and dental caries, reference may be made to the recent literature.[13]

The method of study used in the present investigation is in general similar to that of MacKay and Rose[1] in that the conclusions are based on a series of observations made on children of school age whose early history with regard to rickets was known. It is obviously different from that of the clinical investigators just cited[14] since it does not involve the problem of the adequacy of the diet at the time of the follow-up examinations.

During the years 1923 to 1926 a study of the community control of rickets was carried out in a district of New Haven by the United States Children's Bureau in collaboration with the pediatric department of the Yale School of Medicine. In this study 480 infants were followed from the time the birth certificate was filed until they had reached, in most cases, an age of from 12 to 36 months. During this period antirachitic treatment was given in the form of cod liver oil and sun baths, and progress records were kept by means of roentgen and physical examinations made at frequent intervals during the period of observation. In addition, there were examined over 1,000 infants and young children

10. Mellanby, M., and Pattison, C. L.: The Influence of a Cereal-free Diet Rich in Vitamin D and Calcium on Dental Caries in Children, Brit. M. J. **1**: 507, 1932.

11. Sprawson, E.: The Influence of Raw Milk on Teeth, J. Dent. Research **12**:557, 1932.

12. Report of the Committee upon Dental Disease: The Influence of Diet on Caries in Children's Teeth, Medical Research Council, Special Report Series, no. 159, London, His Majesty's Stationery Office, 1931.

13. Rosebury, T.: The Problem of Dental Caries, Arch. Path. **15**:260 (Feb.) 1933. Agnew, M. C.; Agnew, R. G., and Tisdall, F. F.: The Production and Prevention of Dental Caries, J. Pediat. **2**:190, 1933. Bunting, R. W.: A Review of Recent Researches on Dental Caries, J. Am. Dent. A. **18**:785, 1931. Enright, J. J.; Friesell, H. E., and Trecher, M. O.: Studies of the Cause and Nature of Dental Caries, J. Dent. Research **12**:759, 1932.

14. Footnotes 5 to 12, inclusive.

who had received no cod liver oil, or essentially none, and no sun baths previous to examination. That follow-up examinations of children from these two groups would furnish interesting data with regard to the effect of rickets on skeletal and dental development was obvious.

PRESENT INVESTIGATION

In the period from November 1931 to December 1932, inclusive, 451 of these children were brought back to the clinic for physical, including dental, examinations. In order that the results might show as sharp contrasts as possible, effort was made to reexamine, first, a group of children who had received the most intensive antirachitic treatment and who were known, because of frequent roentgen examinations during the first year or two of life, to have been free or essentially free from rickets and, secondly, a group of children who were definitely

TABLE 1.—*Race, Sex and Age of Children at Recent Examination*

Race and Sex	Total	Age in Years							
		5	6	7	8	9	10	11	12
Total	451	7	115	159	98	28	20	15	9
White Children									
Total	313	5	75	121	71	17	11	7	6
Boys	166	4	35	66	38	7	7	5	4
Girls	147	1	40	55	33	10	4	2	2
Colored Children									
Total	138	2	40	38	27	11	9	8	3
Boys	83	1	20	24	15	7	7	7	2
Girls	55	1	20	14	12	4	2	1	1

known from roentgen examinations to have had moderate or severe rickets. In addition a third group was seen, namely, those who when examined in early childhood showed evidence on clinical examination of having had rickets of moderate degree even though roentgenologic evidence was not at the time present. The present report deals primarily with the condition of the permanent teeth at the time of these follow-up examinations and the relation of the defects found to the diagnoses of rickets made in early life.

Table 1 shows the race, sex and age of the 451 children who were examined. It will be seen that most of the children in each sex and racial group were 6, 7 or 8 years of age at the time of reexamination. A larger proportion of the colored boys than of the other groups were 9 years of age or over, owing to the inclusion in this group of a number of children who were from 2 to 5 years of age when the diagnosis of severe rickets was made. For the study of the incidence of dental caries in the first molars and its relation to race and to the early diagnosis of rickets, only children 6, 7 and 8 years of age were used. For the study

of hypoplastic defects—defects that are produced in the early years of the child's life—the age of the child at the time of follow-up examination was considered of less significance, and the total group from 5 to 12 years was used.

Table 2 shows the classification of the children according to the early diagnoses of rickets and according to race. In the first group are 215 children who were known to have had slight or no rickets; in the second, 108 who from clinical examination were thought to have had moderate rickets, and in the third, 128 who were definitely known by roentgenologic evidence to have had severe or moderate degrees of rickets. In the third group are included 4 children who on clinical examination showed marked bony deformities, but who by roentgen examination were known to have passed the active stage of the disease. As would be expected, a larger proportion of the children in the group with severe rickets were colored.

TABLE 2.—*Degree of Rickets Found in Early Life in Children of Each Race*

Diagnosis of Rickets Made in Early Life	Total Group	Race	
		White	Colored
Total	451	313	138
No rickets or minimum degree by roentgen and clinical diagnosis	215	154	61
Moderate rickets by clinical diagnosis (roentgenologically, none or minimum degree)	108	82	26
Severe or moderate rickets by roentgen diagnosis	128	77	51

At the physical examinations special care was taken to detect the presence of skeletal deformities resulting from the early disease. This was done, not only to determine the ultimate effect of rickets of different degrees of severity on skeletal development, but to compare the incidence of skeletal deformities with that of certain types of dental defects. The upper chart in figure 7 shows the severity of present rachitic deformities of the skeleton in relation to the diagnosis of rickets made in infancy or early childhood. The effect of early antirachitic treatment on the skeletal development is here very apparent, since the group with no rickets is made up largely of children who were given intensive antirachitic treatment in infancy, and the group with severe rickets, of children who were known to have had little if any such treatment.

At the dental examinations the teeth of these children were investigated with special reference to dental caries and to those developmental enamel defects known as enamel hypoplasia. The incidence and location of both types of defects were recorded for each tooth, and the defects were graded as slight, moderate or marked.

A tooth was considered to be carious when there were necrosis and débris associated with cavitation in that portion of the tooth exposed in the oral cavity. An attempt was made to differentiate between active and arrested caries. Differences in physical characteristics, such as the color, hardness and form of the lesion, were used as a basis for making this differentiation, but report of this aspect of the study must await additional examinations of the group and further study of this type of lesion.

The enamel hypoplasia found was characterized first, by a partial lack of enamel, evidenced by thinning, pitting, cupping or grooving; second, as a rule, by a symmetrical distribution of the defects involving those portions of the enamel which were being laid down during the period of injury, and third, by the usual involvement of permanent incisors, cuspids and first molars. The grade recorded for each case of enamel hypoplasia depended on the area of involvement in each of the

Fig. 1.—Photograph (life-size) of the teeth of a Negro child, aged 9 years, who at the age of 2 years had moderately severe rickets in an advanced stage of healing.

affected teeth, the depth of the defect in the enamel and the number of teeth involved.

Figures 1 to 6 illustrate the usual distribution of these hypoplastic defects and some of the variations in the areas involved.

Figure 1 is a photograph of the teeth of a Negro child 9 years of age who when 2 years old had moderately severe rickets in an advanced stage of healing. The defects seen in the teeth are fairly representative of the group in regard to the characteristics of enamel hypoplasia, and the distribution of defects in individual teeth and in the teeth as a whole is the one commonly seen. The defects are symmetrically distributed over those parts of the enamel which were being laid down during the period of injury. In addition to the eight incisors seen in the photograph, the four first molars of the permanent dentition were also involved. The permanent teeth most

commonly affected include the four permanent cuspids, and it is to be expected that in this case they will show similar defects on eruption. A cupped area may be seen on the labial surface of the lower left deciduous cuspid, a defect not infrequently noticed in deciduous cuspids. The enamel between the lines of the defects seen in the upper central incisors seems to extend beyond the normal contour of the crown. This apparent overgrowth was observed in other instances. The pitting and cupping of the enamel along horizontal lines is well illustrated in the photograph. There is typical incisal edge involvement of the upper lateral incisors. The enamel of the affected teeth appears normal near the gingival margin, and those portions of the crowns seem to have full form and contour.

Figure 2 shows the teeth of an Italian child 11 years of age who when 8 months old had severe rickets and tetany. At 4 years of age she was seen again and still showed severe active rickets. At the time of

Fig. 2.—Photograph (life-size) of the teeth of an Italian child, aged 11 years, who when 8 months old had severe rickets and tetany.

examination she had twenty-five permanent teeth, all of which showed marked hypoplastic defects. Figure 3 consists of photographs of a stone model of this child's teeth. Since the premolars and the one second molar that had erupted were also grossly defective, it seems evident that the disturbance responsible for the defects had been operative over a number of years, corresponding reasonably closely with the period in which the child is known to have had rickets.

Figure 4 shows a similar distribution of defects in a colored boy 10 years old who is known to have had severe untreated rickets during the first year of life, with convulsions at 10 months. The very slight involvement of the incisal edge of the upper lateral incisors is in marked contrast to the extensive involvement of the upper central incisors, the four lower incisors and the canines. His first molars were also defective. This distribution is the usual one found in the rachitic children. The disturbance responsible for the defects probably began early in the first year of life. The relatively slight involvement of the upper lateral

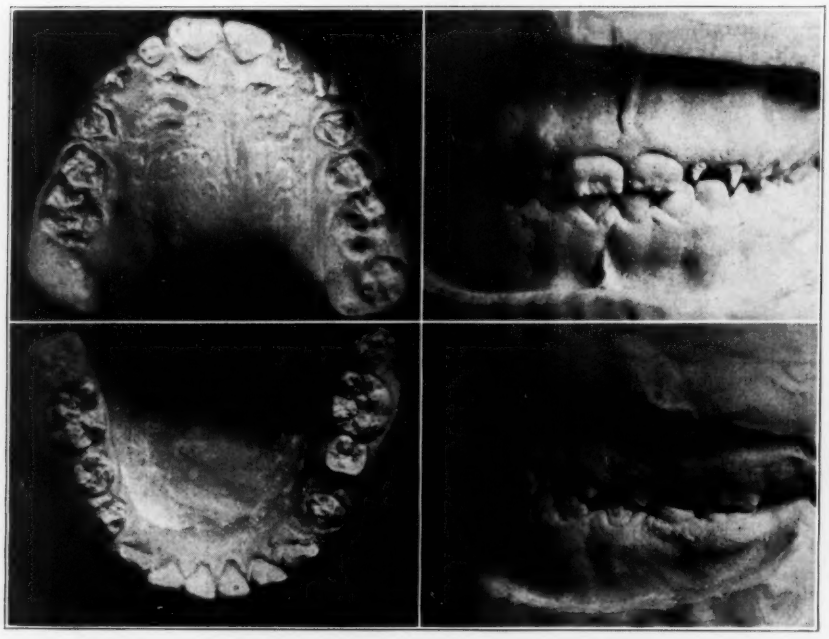

Fig. 3.—Photograph of a stone model of the teeth shown in figure 2.

Fig. 4.—Photograph (life size) of the teeth of a Negro boy, aged 10 years, who had severe, untreated rickets during the first year of life.

incisors and the absence of defects in the premolars suggest that the disturbance probably ceased some time during the second year.

Figures 5 and 6 show variations in the type and severity of defects and in the time when the disturbance probably occurred. They both depict teeth of severely rachitic children. Figure 6 shows two zones of hypoplasia.

A detailed analysis has been made of the incidence of hypoplastic defects of the enamel and of dental caries both in the total group of children examined and in each of the different types of teeth, that is,

Fig. 5.—Photograph (life size) of the teeth of a child with severe rickets.

Fig. 6.—Photograph (life size) of the teeth of a child with severe rickets. Note the two zones of hypoplasia.

in the incisors, molars, cuspids and bicuspids. Of the total group of 451 children studied, 68, or 15 per cent, showed some degree of hypoplastic defect in the enamel of their permanent teeth, and 241, or 53 per cent, showed some degree of caries in one or more permanent teeth. The percentage of children showing hypoplasia is higher than would be expected in a random sample of children in New Haven, since more than half of the group were selected for examination because of their early history of rickets.

The middle chart in figure 7 shows the incidence and degree of the hypoplastic defects among these children after they were classified, as

in the upper chart, into three groups according to the diagnoses of rickets made in infancy or early childhood. It will be seen that 34 per cent of the children known to have had severe rickets showed hypoplastic defects of the enamel, 21 per cent to a severe degree. In contrast, only 4 per cent of the children in the group with no rickets showed hypoplastic defects, and in each of these cases the defects were of a slight or very slight degree, sometimes being found in a single tooth.

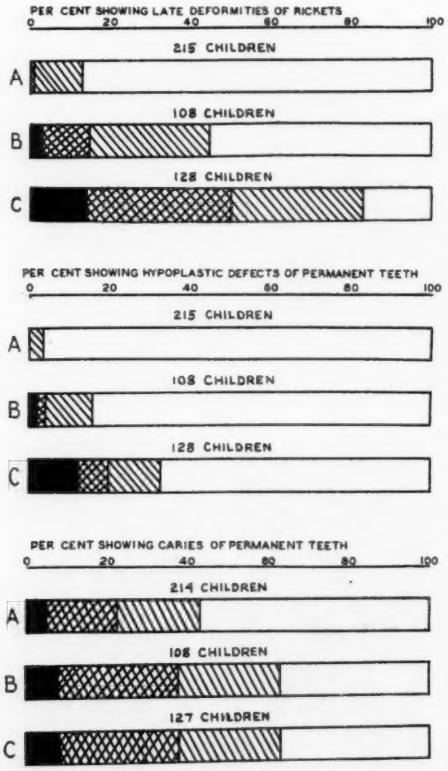

Fig. 7.—Incidence and severity of late rachitic deformities shown on follow-up examination, hypoplastic defects of the enamel and dental caries in 451 children (449 for dental caries) classified in three groups according to the degree of rickets diagnosed in early life. The bar diagrams marked *A* represent the children who in early life did not show rickets on clinical or roentgen examination; those marked *B*, the children who showed moderate rickets clinically but none or a minimum degree roentgenologically; those marked *C*, the children who showed severe or moderate rickets roentgenologically. In all of the diagrams, the degree of severity of rachitic deformities, hypoplastic defects and caries is indicated as follows: severe, by solid black; moderate, by cross-hatching; slight, by diagonal lines, and none, by white.

Table 3 shows in greater detail the relation between the hypoplastic defects found in this group of children and the early diagnoses of rickets. It may be seen that, in general, the more severe the hypoplastic defect, the more often was it associated with severe rickets. There appears to be little doubt that hypoplastic defects of the type described in this paper are usually associated with rickets in early life. When the defects were severe, our experience showed that rickets had always been present.

The question of the relation between caries of the permanent teeth and rickets in infancy is, of course, quite different from that of the relation between hypoplasia and rickets because of the length of time that elapses in most cases between the activity of the rachitic process and the beginning of the carious one. The lower chart in figure 7 shows

TABLE 3.—*Relation of Degree of Hypoplastic Defects to Degree of Rickets Found in Early Life*

		Hypoplastic Defects						
		Children Having No Defects		Children Having Defects				
				Total		Degree of Defect		
Degree of Rickets	Total	Number	Per Cent	Number	Per Cent	Slight	Moderate	Marked
Total	451	383	100	68	100	38	12	18
No rickets or minimum degree by roentgen and clinical diagnosis	215	207	54	8	12	8	..	..
Moderate rickets by clinical diagnosis (roentgenologically, none or minimum degree)	108	91	24	17	25	13	2	2
Severe or moderate rickets by roentgen diagnosis	128	85	22	43	63	17	10	16

the incidence of caries in the same three groups of children represented in the upper and middle charts, classified on the basis of the diagnoses of rickets made in early life. The contrasts here are less striking, but the difference between the incidence of caries in the group without rickets (43 per cent) and that in the group with severe rickets (63 per cent) is, in all probability, significant and indicates that, at least as far as these children are concerned, caries was more apt to occur in the permanent teeth of children who had had severe rickets in infancy than in those of children who had not. The greater number of hypoplastic defects found in the teeth of the children who had had severe rickets in infancy and the consequent increased number of areas for the mechanical lodgment of food and débris may well account for the increased incidence of caries in this group on a purely mechanical basis.

Study of the incidence of these two kinds of dental defects in the different types of permanent teeth showed that, in accord with the usual

experience, the hypoplastic defects of the enamel occurred considerably more often in the incisors and caries occurred much more often in the first molars. Figure 8 shows the percentage of hypoplasia and of dental caries in the upper and lower incisors and in the first molars of the total group of children. It should be pointed out that the proportions of defects in the cuspids and bicuspids are not shown because few of the children were old enough to have these teeth. The greater incidence of hypoplastic defects in the upper incisors than in the lower, and the greater incidence of caries in the lower molars than in the upper, should also be noted.

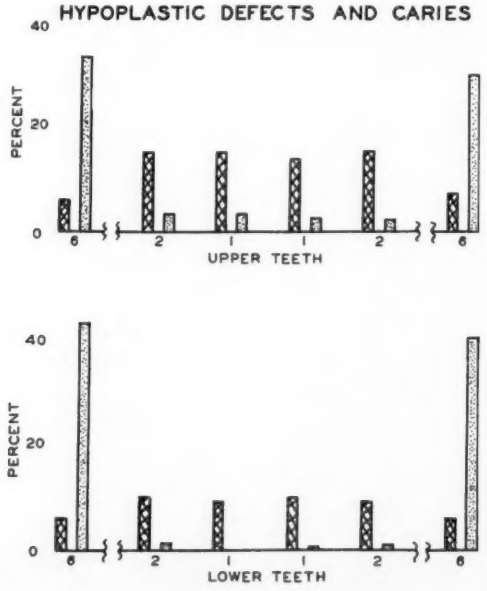

Fig. 8.—Incidence of hypoplastic defects (indicated by cross-hatching) and of caries (indicated by dots) in the permanent incisors and first molars of 451 children. Central incisors are indicated by *1*, lateral incisors by *2*, and first molars by *6*.

A and *B* in figure 9 show, respectively, the differences in the incidence of hypoplastic defects and of dental caries in the incisors and the first molars when the children are grouped on the basis of the early diagnoses of rickets. In figure 9 *A* the contrast between the proportion showing hypoplastic defects in the group without rickets and that in the group with severe rickets is striking for each type of tooth. It is evident that hypoplasia was many times more common in the teeth of children who had had rickets. The contrast, as shown in figure 9 *B*, between the proportion of first molars showing dental caries in the group without rickets and that in the group with severe rickets is less

striking, but the differences are nevertheless great enough to be significant. These data derived from study of individual types of teeth bear out, in general, the conclusions drawn from the study of the total incidence of the defects in the groups of children shown in figure 7.

The differences in the incidence of hypoplastic defects and of dental caries in the incisors and first molars of white and colored children are shown in figure 10. The higher percentage of hypoplasia among the colored children (fig. 10 *A*) is striking. If the relation of hypoplasia to rickets is studied for the white and colored children separately, the general relationships shown in figure 9 *A* for the total group are found to hold true for each racial group, indicating that the disease rather than the racial factor is the more important. Figure 10 *B* shows the usual picture of the incidence of caries in the first molars of white and colored children. Again, if the racial factor is eliminated by studying each group separately, it is still found that caries was present more often in the molars of children who gave a history of severe rickets in early life than among those who did not.

In order to throw further light on this question of the relation of caries in the permanent teeth to rickets in early childhood, we have compared the incidence of caries in the hypoplastic and the nonhypoplastic teeth, studying the incisors and the first molars separately because of the difference in the incidence of caries in these teeth. Table 4 shows these comparisons. Caries was found in 50 per cent of the molars that were hypoplastic, whereas it was found in only 36 per cent of those that were not. Moreover, though the incidence of caries is very small in all incisors (only 2 per cent), it was found in 4 per cent of those that were hypoplastic and in only 1 per cent of those that were not. These data tend to bear out the statement of Mellanby [15] that caries occurs more often in teeth that are structurally defective and to corroborate to some extent the findings of the British Medical Research Council in their study of "The Incidence of Dental Disease in Children." [16] The latter investigators found that caries developed twice as often in grossly hypoplastic teeth (26 per cent) as in normal teeth (13 per cent). Though our data show that caries develops more often in hypoplastic than in nonhypoplastic teeth, they do not demonstrate a causal relationship between the two conditions.

The fact that severe infections may possibly play some rôle in the production of enamel hypoplasia or that rickets accompanied by tetany

15. Mellanby, M.: The Structure of Human Teeth, British Dent. J. **48**: 1481, 1927.

16. Report of the Committee for the Investigation of Dental Diseases: II. The Incidence of Dental Disease in Children, Medical Research Council, Special Report Series, no. 97, London, His Majesty's Stationery Office, 1925.

may be a more significant etiologic factor than rickets alone has not been overlooked in studying this group of children.

Our data show that children who have had several of the severe infectious diseases of childhood (including pneumonia and bronchitis)

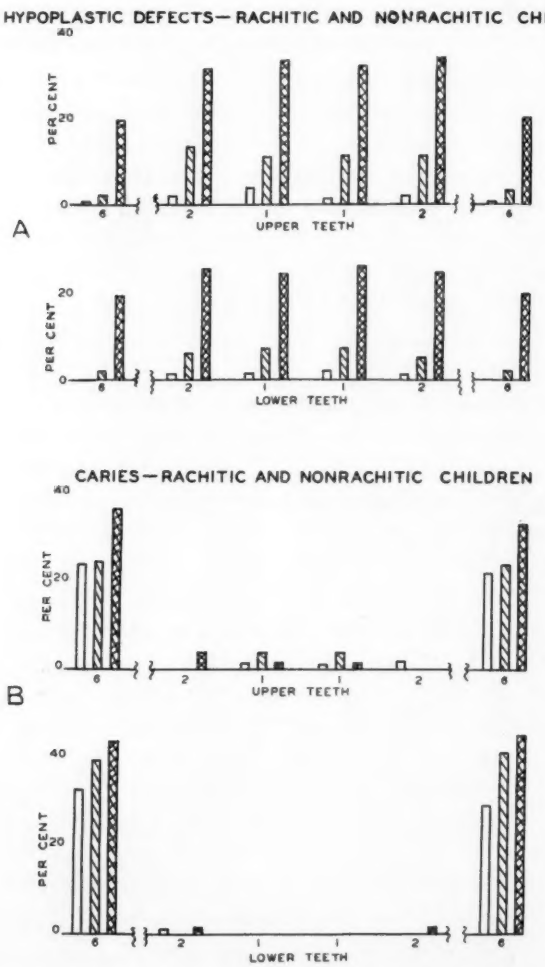

Fig. 9.—*A* shows the incidence of hypoplastic defects in the permanent incisors and first molars of 451 children grouped according to the early diagnosis of rickets. *B* shows the incidence of caries in the permanent incisors and first molars of 372 children (6 to 8 years of age) grouped according to the early diagnosis of rickets. The white spaces indicate no rickets; the diagonal lines, moderate rickets (clinically), and the cross-hatching, severe or moderate rickets (roentgenologically).

tend to have defects in the enamel more often than children who have had fewer of these diseases. With respect to this finding, it seems

reasonable to suppose that interference with the normal formation of enamel may well occur more frequently and the injury be greater when a severe infectious disease is superimposed on a rachitic process. Whether the infectious disease produces the hypoplastic defects or

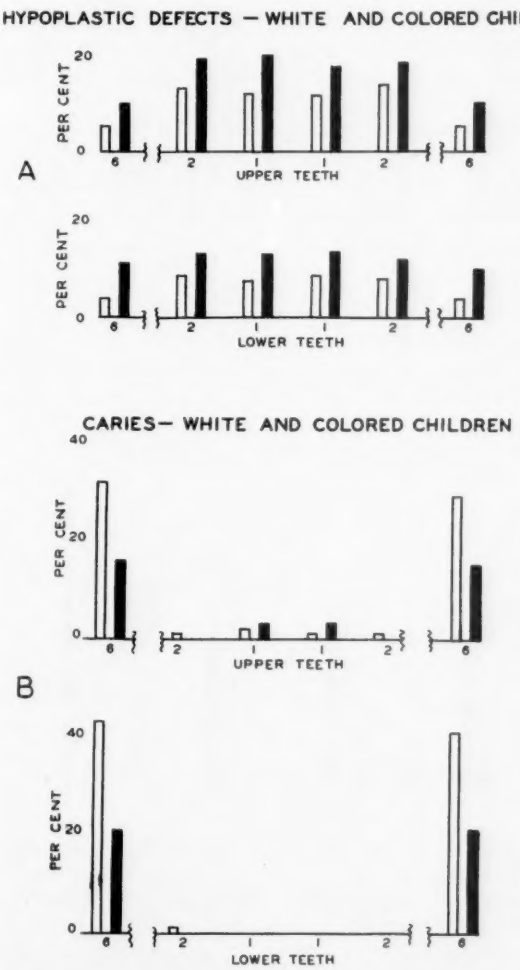

Fig. 10.—*A* shows the incidence of hypoplastic defects of the permanent incisors and first molars in 313 white and 138 colored children. *B* shows the incidence of caries of the permanent incisors and first molars in 267 white and 105 colored children (6, 7 and 8 years of age). The white spaces indicate white children; the black ones, colored children.

merely increases a disturbance of mineral metabolism already present and so indirectly produces the defects cannot be demonstrated from our data, but the latter view seems to be the more likely.

From the data available, it has not been possible to show a definite relation of hypoplastic defects to tetany, but a considerably higher incidence of convulsions occurring in children under 3 years of age with hypoplasia (22 per cent) as compared with the incidence in children with no hypoplasia (6 per cent) is of interest in this connection. It may be pointed out, however, that in the case of a number of children who

TABLE 4.—*Incidence of Caries in Hypoplastic and Nonhypoplastic First Molars and Incisors (Permanent Teeth)*

	Total Number of Teeth	Carious Teeth	
		Number	Per Cent
First Molars:			
Total examined	1,603	583	36
Hypoplastic	101	50	50
Nonhypoplastic	1,502	533	36
All Incisors:			
Total examined	2,399	35	2
Hypoplastic	281	11	4
Nonhypoplastic	2,118	24	1

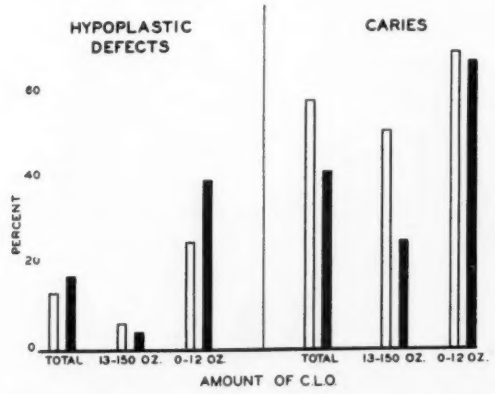

Fig. 11.—Incidence of hypoplastic defects and caries of the permanent teeth in relation to the amount of cod liver oil received in infancy in 309 white and 123 colored children. The white spaces indicate white children; the black ones, colored children.

showed severe hypoplastic defects a definite diagnosis of tetany had been made in infancy from blood studies.

One other aspect of the study which is perhaps self evident from the foregoing data, but which is of considerable interest from a preventive point of view, is the relation of hypoplastic defects or of dental caries to the administration of cod liver oil in infancy. Figure 11 shows these relationships for white and colored children separately and, as would be expected, indicates clearly that hypoplastic defects may be largely

prevented by antirachitic therapy in infancy and early childhood. The effect on the incidence of caries is, as would also be expected, much less striking.

CONCLUSIONS

It appears from the data here presented that enamel hypoplasia of the permanent teeth, especially the type that is characterized by a symmetrical distribution of defects in those teeth which are forming during infancy and early childhood, is frequently associated with rickets. It has been shown that the more severe the rachitic process the more frequently do hypoplastic defects develop; conversely, when severe hypoplasia was found, a definite history of moderate or severe rickets was established in practically all cases by roentgenologic evidence.

Dental caries too was found more often in children with a known history of rickets, but since the data also indicate that caries was found more often in teeth with hypoplastic defects than in those with none, it is possible that the latter relationship may account for the former.

That the administration of antirachitic therapy in infancy reduces the incidence of enamel hypoplasia and also to some extent lessens the incidence of caries has been shown.

OSTEOMYELITIS OF THE MAXILLA IN NURSLINGS AND IN INFANTS

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An extensive literature has grown up around the subject of osteomyelitis of the maxilla in nurslings and infants. The clinical picture has been described under a varied terminology, and many factors have been ascribed to its causation. The onset of the disease has varied from the first week to the ninth month of the infant's life, but the greatest number of cases on record have occurred within the first few weeks of the neonatal period. The basic clinical picture has been strikingly uniform, with redness, swelling, purulent discharge, necrosis and sequestration of the maxilla on one or all of its surfaces (nasal, orbital, facial and palatal). The points of entry, the method of spread of the invading organism and the clinical course have varied greatly, however.

The subject has been extensively reviewed and summarized in the American literature twice within recent years in articles by Bass [1] and Wilensky.[2] It would be needless repetition to consider again in detail the different opinions which have been held of the pathogenesis of this disease. In the early medical literature [3] practically all the cases were classified under empyema of the antrum. In 1904, Brown Kelly [4] reviewed seventeen cases listed under sinus disease in infants, and attempted to establish the symptom complex under the diagnosis of osteomyelitis of the maxilla, as Smiegelow [5] had done eight years before. He pointed out that the structure of the maxilla in infancy, with its numerous foramina and dental sacs, would lend itself to the rapid extension of an inflammatory process to one or more of its surfaces. During the same year, Swoboda [6] called attention to the tooth anlage as a start-

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1. Bass, M. H.: Acute Osteomyelitis of the Superior Maxilla in Young Infants, Am. J. Dis. Child. **35**:65 (Jan.) 1928.

2. Wilensky, A. O.: Pathogenesis and Treatment of Acute Osteomyelitis of Jaw in Nurslings and Infants, Am. J. Dis. Child. **43**:431 (Feb.) 1932; Osteomyelitis of the Jaws, Arch. Surg. **25**:183 (July) 1932.

3. Mayer, E.: M. Rec. **60**:210, 1901.

4. Kelly, B.: Edinburgh M. J. **16**:302, 1904.

5. Smiegelow, quoted by Kelly.[4]

6. Swoboda, quoted by Zarfl.[8]

ing point for osteomyelitis of the maxilla in nurslings. Since that time a number of causes has been assigned to the pathogenesis, and each writer has sought to establish the underlying mechanism.[7]

Few of the cases reported have been studied histologically, and it has been difficult to determine accurately the mechanism of the disease solely by clinical study. The patients are too often seen after the pathologic process is well established, and consequently the primary seat of the process can only be inferred. The object of this communication is to present the results of a combined clinical and histologic study of a case commonly referred to in the literature as acute osteomyelitis of the maxilla, with the hope that similar cases will be viewed with these facts in mind.

REPORT OF A CASE

History.—R. B., a white male infant, was admitted to the hospital at the age of 3 weeks. The mother stated that nine days before admission the infant had a marked thick, yellow, nasal discharge. The infant was restless and refused to nurse. Fever was not present at this time. Two days later the nasal discharge became thin and mucoid, and coincident with this the left eye became reddened and a swelling appeared on the upper eyelid. In the next twenty-four hours the lower eyelid became swollen. Forty-eight hours later the child was taken to a doctor, at which time a point of swelling was noted on the left upper margin of the gum. The next day there was a spontaneous discharge of thick, bloody, purulent material from the left nostril. This was followed by a progressive decrease in swelling about the eyelids. The day before admittance several small fluctuant areas developed on the left cheek near the outer angle of the eye, and the lids again became edematous. Because of this the patient was brought to the hospital. The mother believed that the infant was afebrile throughout the entire course of the illness.

The patient was the second child of healthy parents. The mother was in labor three hours and had a normal, spontaneous delivery. The immediate neonatal history was normal, and the patient did well until the present illness.

Physical Examination.—The patient was a fairly well nourished infant. He did not appear acutely ill, but was restless and irritable. No eruptions or lesions were present on the surface of the body. Positive physical findings were confined to the head. The left side of the face was prominent and asymmetrical. The left eyelid was reddened and edematous, and the left eye was almost closed. The edema of the eyelids extended beyond the outer canthus of the left eye almost to the temporal region (fig. 1). A scant seropurulent discharge drained from the inner canthus of the left eye. A sanguinopurulent discharge exuded from the left nostril, reappearing rapidly when wiped away. Pressure on the left maxilla increased the discharge from the left nostril. On examination, the material appeared to come from below the inferior turbinate. The right nostril was clear. The left alveolar margin was swollen and boggy. A fistulous opening was present in the region of the first molar tooth. A thick yellow discharge drained from this area, and was increased by pressure over the left maxilla. The pharynx was diffusely hyperemic throughout. The entire left cervical group of lymph glands

7. Bronner, H.: Beitr. z. klin. Chir. **133**:163, 1925. Marx, E.: Brit. J. Ophth. **6**:25, 1922. Paunz, M.: Ztschr. f. Hals-, Nasen- u. Ohrenh. **13**:155, 1926.

was enlarged and firm. The left cheek and mandible were swollen and soft. The overlying skin had a faint purplish-red color.

Laboratory Data.—The urine was normal. Examination of the blood showed: hemoglobin, 68 per cent (Newcomer); red blood cells, 2,970,000, and white blood cells, 13,650, with a differential count of 49 per cent polymorphonuclears, 47 per cent lymphocytes, 3.5 per cent monocytes and 0.5 per cent eosinophils. A culture of the discharge from the left side of the nose, the left eye, and the fistula showed Staphylococcus aureus.

Course.—The temperature on admission was 99 F., but rose progressively to 103 F. on the fourth day. Coincident with this rise, there was an increase in the swelling and fluctuation in the areas mentioned. A few fistulas developed on the left side of the face just outside the outer canthus of the left eye. The swelling

Fig. 1.—Photograph of the patient, showing orbital edema and swelling of the left side of face. Fluctuant areas are visible at the outer angle of the left eye.

in the neck increased and extended to the zygoma. The patient did not respond to supporting measures and died six days after entrance. Postmortem examination revealed that the patient died of terminal bronchopneumonia.

Histologic Observations.—A special histologic study of the head was made by Dr. Blayney. The histologic sections revealed changes in complete accord with the clinical symptoms. A section in the frontal plane in the region of the deciduous molar (fig. 2) showed an old extensive osteomyelitis of the inferior turbinate, also a more recent involvement of the maxillary sinus. At *A* (fig. 2) was the crypt of the deciduous molar which was lost in sectioning. There was a break in the lower border of the maxillary sinus, with a fistulous tract leading downward and dividing at *B*, one division extending outward to a large abscess in the cheek while the other portion progressed downward into the oral cavity.

A careful survey was made of the soft tissue covering the tips of the enamel cusps and incisal edges of the deciduous teeth. In each case there was a sufficient pad of soft tissue between the oral epithelium and the crown of the tooth to preclude the possibility of the laceration of this tissue and the exposure of the tooth germ during the cleansing of the mouth immediately after birth. It is evident that the involvement of the inferior turbinate was considerably older than that seen in the other regions of either the maxilla or the mandible. This strongly suggests that the original infection was of nasal origin.

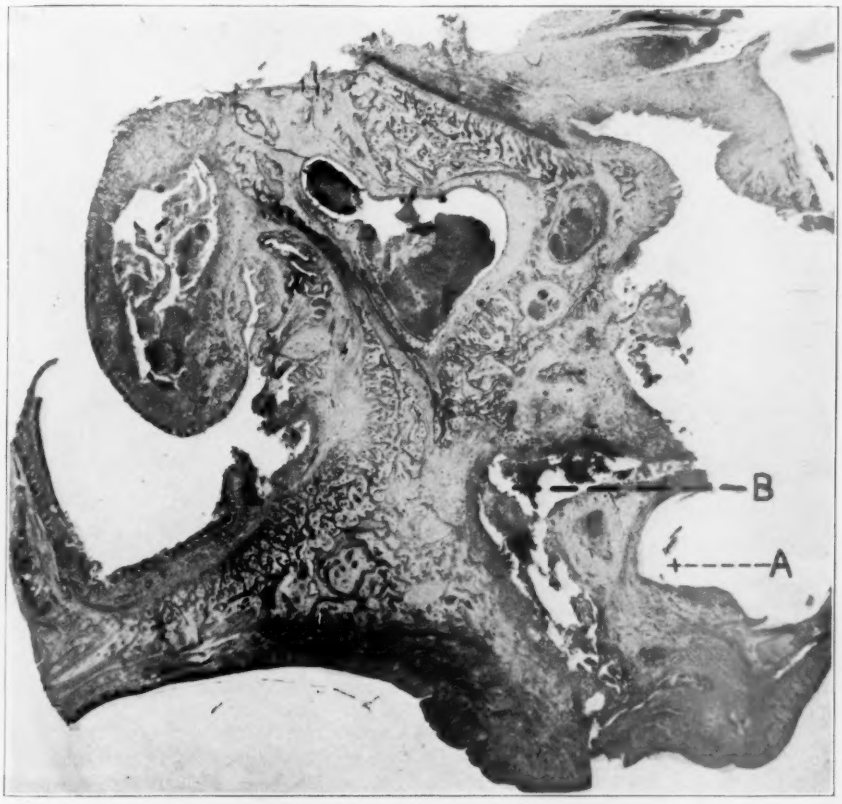

Fig. 2.—Frontal plane section in the region of the deciduous molar, showing old extensive osteomyelitis of the inferior turbinate and pus in the maxillary sinus. *A* shows the crypt of the deciduous molar, and a necrotic focus (*B*) resulting from a fistulous tract from the maxillary sinus. From the area (*B*) the fistulous tract can be seen to divide toward the cheek and downward into the oral cavity.

Figure 3 shows a section in the frontal plane in the region of the first permanent molar. At this level the facial wall of the sinus was completely destroyed; a large fistulous tract, containing spicules of exfoliated bone, led into the abscesses in the cheeks and a finger-like projection reached downward external to the tooth germ. The zygomatic wall of the antrum had been destroyed by extension of the process into the sphenomaxillary fossa. There were two smaller abscesses in

the immediate vicinity of the maxillary division of the fifth nerve, and also a small abscess immediately beneath the lateral wall of the nasal cavity. In the sphenomaxillary fossa was a small abscess with septic thrombi in some of the nearby veins. Figure 4 shows a plane just anterior to the distal wall of the pharynx, and includes the body of the sphenoid, the basilar process, the cavernous sinus, the internal carotid artery (*I.C.A.*) with the associated nerve trunks and ganglions and a portion of the greater wing of the sphenoid. In the cavernous sinus were several septic thrombi (*S.T.*). The extension from the antrum through the maxilla was not limited to the distal direction, as extensive involvement of the structures was found immediately above the deciduous central incisor and cuspid; however, the soft tissue between the oral cavity and the tooth crown was normal and unbroken.

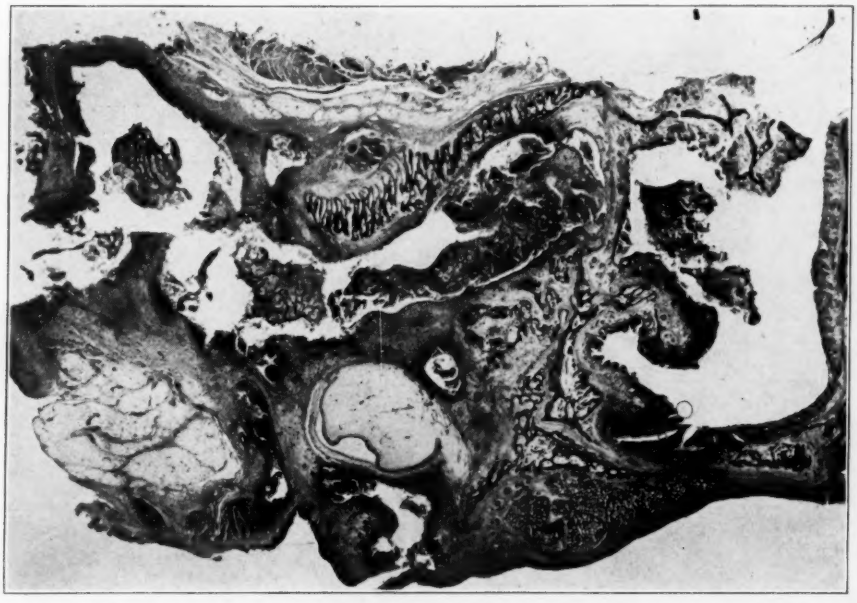

Fig. 3.—Frontal plane section in the region of the first permanent molar. The photomicrograph is reversed and should be viewed from right to left. The facial wall of the maxillary sinus is destroyed and is continuous with a large fistulous tract the tributaries of which are shown in figure 2, pointing to the cheek and oral cavity.

In the study of the mandibular sections, osteomyelitis was found extending forward from the mandibular foramen to the region of the deciduous cuspid. The degree of reaction and the amount of destruction of the tissue were much more pronounced in the maxilla than in the mandible. At the time of autopsy the mandible was separated from the maxilla; therefore, it was impossible to trace the spread by direct continuity. However, in a section through the mandibular foramen, the abscess was seen to enter the body of the lower jaw along with the mandibular vessels and nerve. Since the zygomatic wall of the sinus was destroyed, and the content entered the sphenomaxillary fossa, it is easily understood how

the spreading could occur along the planes of the buccal fascia and the pterygoid muscles and following the sheaths of the third division of the fifth nerve and the inferior dental artery enter the lower jaw through the mandibular foramen.

In the region of the first permanent molars was a large abscess immediately beneath the dental pulp and in close proximity to the mandibular nerve. Inferior to this, the major portion of the original mandibular bone was involved in an ostemyelitic process. The body of the mandible was completely surrounded by a formation of new bone with the trabeculae arranged at right angles to the surface.

Fig. 4.—Frontal plane section just anterior to the distal wall of the pharynx. *I.C.A* is the internal carotid artery and *S.T.* indicates septic thrombi in the cavernous sinus.

This arrangement of the trabeculae did not exist on the opposite side and suggested an effort on the part of nature to withstand internal pressure. A deciduous molar is shown in figure 5. There was a large area of destruction and a spreading of the process along the lateral wall of the tooth with complete destruction of the enamel organ on the occlusal surface, although the overlying soft tissue was intact.

Throughout the entire mandibular series there was not a trace of the inferior dental artery posterior to the cuspid region. This fact seems to support the

statement that the infection entered the lower jaw by extension along the vessel sheath, ultimately destroying it, and that the involvement of the lower jaw was not the result of thrombophlebitis. In the anterior region of the mandible the structures took on their normal appearance and arrangement. Nowhere was there evidence of destruction of tissue, and the arrangement of the trabeculae was normal.

Summary of Observations.—The clinical course in this case is apparent after studying the serial sections of the entire head. There is incontestible evidence that the original site of entrance was in the inferior turbinate. The osseous

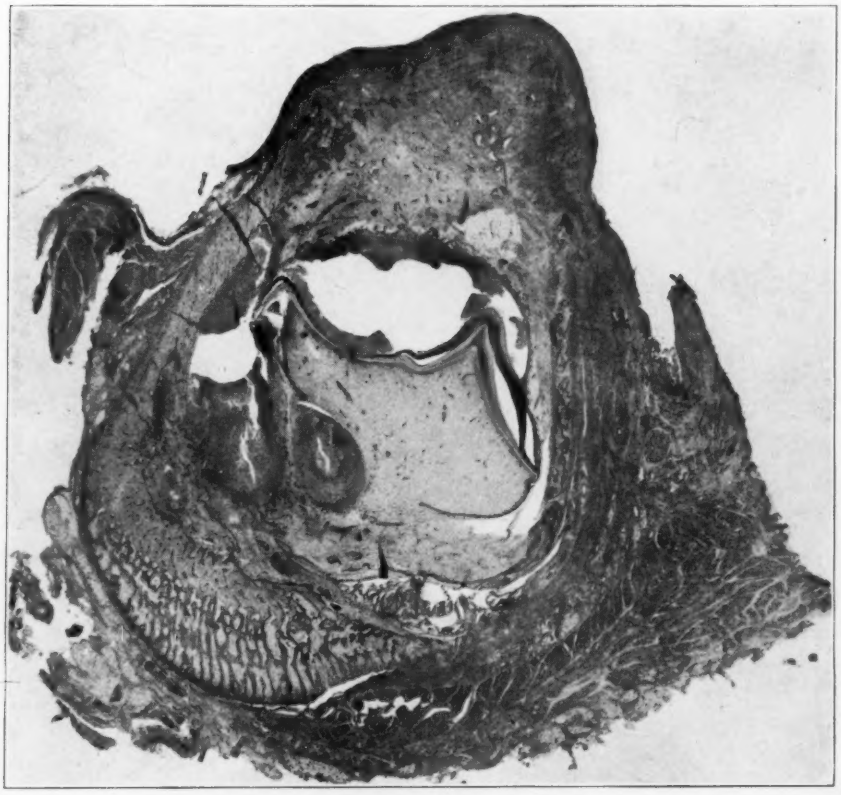

Fig. 5.—A section through the body of the mandible in the region of the deciduous molar. At the left lateral wall of the tooth is a large necrotic focus which spread to the occlusal surface of the enamel organ. Beneath the area of destruction, formation of new bone may be seen with trabeculae arranged at right angles to the surface.

portion of the inferior tubinate was replaced by what almost appeared to be encapsulated necrotic material (fig. 2). This appeared to be the oldest process. The epithelium of the turbinate was almost devoid of cilia, and the mucosa was everywhere intact except in the inferior meatus, where it was destroyed (fig. 2). Following purulent rhinitis and sinusitis there developed periostitis and periorbital cellulitis, which later broke down. From the suppurative process in the maxillary

sinus and the ethmoidal labyrinth septic thrombi invaded the venous channels, producing a cavernous sinus thrombosis (fig. 4). From the original site, the process extended to the maxillary sinus, resulting in a fulminating sinusitis. The exudate in the maxillary sinus caused necrosis which gave rise to a fistulous tract at the floor of the sinus that broke through into the roof of the mouth. The facial surface of the maxillary sinus was destroyed, and the necrotic process extended into the zygomatic arch (fig. 3). This resulted in the formation of abscesses in the soft tissues of the cheek, with sinuses draining to the face and in the sphenomaxillary fossa. The mandible became involved by direct extension along the sheaths of the inferior dental vessels and nerve.

COMMENT

It appears from the study of this case that osteomyelitis of the maxilla in infancy may result in a number of ways. Dogmatic statements regarding the pathogenesis have been made by proponents of each view. Wilensky [2] believed that osteomyelitis of the maxilla in infants differs in no way from osteomyelitis in general and that localization in the jaws in the nursling is due to traumatic factors incident to that period (traumatic conditions of childbirth, cleansing of the mouth, etc.). The predilection for the maxilla is explained by its larger size and its more rigid construction and attachment to the skull, which favors a more frequent reception of trauma. The rôle of the tooth anlage in the disease process is simply as an area of more marked vascularity that might fix a metastatic infection. It was Wilensky's belief that the local clinical manifestations in the maxilla are determined by the dominating position of the thrombophlebitis in the course of the vascular channels supplying the jaws. The dominating clinical manifestation (orbital, nasal, palatal or facial) would depend on the position of the thrombophlebitis and the resulting necrosis.

Zarfl's [8] views on the subject are, however, much more in keeping with the clinical facts of the cases reported. On the basis of a careful histologic study he pointed out that the purulent inflammation does not begin in the tooth anlage itself but in the surrounding tissue, that involvement of the tooth anlage is secondary. On the basis of clinical and histologic observations Zarfl divided his cases into two types: phlegmonous, and osteomyelitic, according to whether the soft parts of connective tissue or bone was primarily involved. Differences in the clinical course are presented that correlate with the underlying pathologic process. The final cause of the disease is the entrance of organisms into the soft parts or bone marrow of the jaw. If the soft parts are involved the pathologic process is phlegmonous. If bacterial emboli lodge in the bone marrow the resulting process is osteomyelitic. The former is usually the result of an inflammatory focus in the region of the jaw; the latter, that of a

8. Zarfl, M.: Ztschr. f. Kinderh. **25**:266, 1920.

distant focus. The cases Zarfl grouped under the phlegmonous type showed circumscribed foci which extended to the jaw by way of the lymph channels (erysipelas of the face and stomatitis). In the osteomyelitic group there was a spread through the blood stream from a distant focus (furuncle, etc.).

After attempting to evaluate the reports of cases and reviewing the facts obtained in the study of our case it appears that the portal of entry of the primary infection and the method of spread may be varied. No one explanation can be used to elucidate the pathologic sequelae in all cases. The infection may travel by direct extension (continuity of structure), by the lymphatics or by the blood stream.

It is our impression that the part played by nasal infection and sinusitis (maxillary and ethmoid) is more important in the pathogenesis of osteomyelitis of the maxilla in infancy than is commonly believed. This etiology has been suggested many times in the literature, but no serious consideration has been given to the views because of the lack of complete development of the sinuses during infancy. At birth, however, the maxillary sinus and ethmoidal cells are always sufficiently advanced in their development to be of clinical importance. The histologic study in this case is corroboration of that statement. The fact that the entire tooth germ is sometimes exfoliated through the draining sinuses in the maxilla does not mean that the tooth anlagen were the original site of the pathologic process or that they are especially liable to such involvement. In our case, despite the marked necrosis, the tooth pulps withstood the destruction remarkably well. The discharge of tooth buds through a draining sinus does mean that the structures supporting them have been destroyed. The portal of entry and original source of this inflammation which give rise to such destruction might well be, and frequently is, in the nose and the paranasal sinuses.

CONCLUSION

The pathogenesis of osteomyelitis of the maxilla in infants is discussed. From the study of reports in the literature it is evident that the portal of entry and the method of spread may be variable. Evidence has been presented to show that nasal infection and sinusitis may play an important rôle in the pathogenesis at an early age period. In the future study of such cases this mechanism should receive adequate consideration.

TUMORS OF THE BRAIN IN INFANCY

CLINICAL AND PATHOLOGIC STUDY

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CLEVELAND

Tumors of the brain in infancy (that is, during the first two years of life) differ from those in later life in several respects. The alteration in intracranial physiology produced by an expanding lesion in an infant, in whom the sutures are ununited and the cranial bones yielding and elastic, differs greatly from the disturbances which result when a similar lesion develops in the closed and unyielding intracranial cavity of an adult. This fact accounts in a large measure for the differences in symptoms produced by tumors of the brain in infancy compared to those produced in adults. Differences in the predominant types of tumors and their sites of predilection in infancy also contribute to a clinical picture which differs in many respects from that seen in older persons suffering from tumors of the brain. The problem of diagnosis presents many features which are peculiar to this age period. While it is true that a gradually increasing defect in nervous function should make one suspicious of an intracranial neoplasm in an adult, this sign is often absent in infancy, at which time the symptoms frequently develop with amazing rapidity. In infancy the localization of a tumor of the brain is especially difficult because the age of the patient precludes the testing of visual fields and sensation and other tests which require the intelligent cooperation of the subject.

REVIEW OF THE LITERATURE

The age incidence of tumors of the brain has been studied by various authors. Cushing, in an article on tumors of the brain of preadolescence [1] and in other reports showed that each epoch of life has certain types of tumors which tend to occur in favored locations. It has long been known that subtentorial growths occur more frequently in children and young adults than in older persons, yet tumors arising from the sheaths of the

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Read at a meeting of the Central Neuropsychiatric Association, Cleveland, Oct. 14, 1933.

1. Cushing, Harvey: The Intracranial Tumors of Preadolescence, Am. J. Dis. Child. **33**:551 (April) 1927.

eighth nerve are almost unknown in childhood, having their greatest incidence in the age period of from 25 to 50.

Because of the relatively infrequent occurrence of tumors of the brain in infants, histologic studies with clinical correlation have rarely been reported. Most textbooks quote the old statistics of Starr,[2] who collected reports of tumors of the brain in 300 persons under the age of 18; 50 per cent of the tumors were said to have been tuberculomas. The statements concerning intracranial neoplasms in infants are vague and often contradictory. The literature contains many reports of tumors of the brain in children, but the occurrence of such tumors in infants has received little attention. Wollstein and Bartlett[3] reviewed 4,563 necropsy records in the Babies' Hospital of the City of New York, and found records of tumors of the brain in only 9 patients under the age of 3. Of these, 7 were studied in detail. Five of the tumors were cerebellar and 2 cerebral. In 1,028 records of conditions diagnosed as "brain tumor" in the National Hospital, London, Critchley[4] found 125 in children up to the age of 16, and only 3 in children up to the age of 3. In Cushing's series,[1] from Oct. 1, 1913, to Oct. 1, 1926, there were 1,108 verified tumors of the brain. Of these, only 24 were in children under 5 years of age. Vogt's[5] monograph on cerebral tumors in children is based on 30 cases in children under the age of 15, but only 14 were verified at operation or autopsy.

There are scattered examples of intracranial neoplasms in infants. Among the early reports is that of Maier,[6] who, in 1861, reported the case of a 10 week old boy who was well up to his sixth week, when he began to have generalized convulsions. He had a large head and the typical facies of hydrocephalus. At postmortem examination a large tumor was found in the left ventricle, arising in the basal ganglions. It was made up of many cysts which varied in size, and on histologic examination proved to be a dermoid. Cayley's[7] case was that of an infant who had been in good health up to the age of 4 months, when he

2. Starr, M. Allen, in Keating, John M.: Cyclopaedia of the Diseases of Children, Philadelphia, J. B. Lippincott Company, 1890, vol. 4, p. 551. Sachs, Ernest: Diagnosis and Treatment of Brain Tumors, St. Louis, C. V. Mosby Company, 1931, p. 180.

3. Wollstein, M., and Bartlett, F. H.: Brain Tumors in Young Children, Am. J. Dis. Child. **25**:257 (April) 1923.

4. Critchley, Macdonald: Brain Tumors in Children, Brit. J. Dis. Child. **22**: 251, 1925.

5. Vogt, Claire: Les tumeurs cérébrales chez l'enfant, Paris, Louis Arnette, 1929.

6. Maier, Rudolf: Combinierte Geschwulst im Grosshirn, Virchows Arch. f. path. Anat. **20**:536, 1861.

7. Cayley, W.: Cyst of the Choroid Plexus, Tr. Path. Soc. London **27**:25, 1876.

was brought to the physician because of persistent vomiting. There had been no convulsions or paralysis, and the fontanels did not bulge. After an illness of ten days the infant died. At postmortem examination a cyst the size of an egg was found in the left ventricle arising from the choroid plexus. The walls of the cyst were thin and translucent, and the cyst contained a clear serous fluid. Steffen,[8] in a discussion of tumors of the brain in childhood, mentioned 2 cases in infants reported in the literature, 1 in a patient of 2 months and the other in a patient of 6½ months. Saxer,[9] in 1896, reported the case of a 7 week old infant who had a teratoma in the third ventricle. The infant was normal up to the age of 4 weeks, when her head began to enlarge rapidly, and a diagnosis of hydrocephalus was made. At autopsy a tumor was found attached to the choroid plexus of the third ventricle. It contained epidermoid elements, muscle and embryonic nerve tissue. Marion's [10] case was that of a male infant of 16 months who was taken ill with a slight fever and vomiting followed by ocular palsy, unsteady gait and enlargement of the head. At autopsy a tumor the size of a walnut was found in the region of the thalamus. There was marked internal hydrocephalus. The histologic diagnosis was glioma. Eliasberg [11] reported the case of a male infant of 18 months who had been well up to one month previous to examination, when he began to have a tremor of the hands followed by vomiting and inability to walk. Autopsy showed the pia of the brain and spinal cord to be infiltrated by a diffuse tumor which was most evident on the under surface of the cerebellum. The tumor cells were small and round, with scanty cytoplasm and deeply stained nuclei. Eliasberg believed the tumor to be a primary sarcoma of the pia. Holt's [12] case was that of a male infant of 7 weeks who had been normal at birth. At about the age of 2 weeks the infant's head began to enlarge rapidly, and persistent vomiting occurred. There was a prominence in the left frontal region, and the veins of the scalp were dilated. Finally, the scalp over the frontal eminence ruptured, producing a cerebral hernia. The infant survived this only two days. At postmortem examination the left hemisphere was found to be greatly enlarged and invaded by

8. Steffen, A.: Geschwülste des Gehirns im Kindesalter, in Gerhardt, C.: Handbuch der Kinderkranheiten, Tübingen, H. Laupp, 1887, vol. 5, p. 545.

9. Saxer, F.: Ein zum grössten Theil aus Derivaten der Medullarplatte bestehendes grosses Teratom im III. Ventrikel, Beitr. z. path. Anat. u. z. allg. Path. **20**:339, 1896.

10. Marion, G. A.: Case of Brain Tumor in an Infant, New York State J. Med. **16**:201, 1916.

11. Eliasberg, H.: Zur Klinik der Rückenmarkserkrankungen im Kindesalter, Jahrb. f. Kinderh. **84**:445, 1916.

12. Holt, L. E.: Gliosarcoma in an Infant, Am. J. Dis. Child. **14**:219 (Sept.) 1917.

a large soft neoplasm containing many old and recent hemorrhages. The diagnosis was gliosarcoma.

Löwenberg's [13] case was that of an infant of 10 months who began to vomit in his ninth month. This was followed by convulsions and drowsiness. At autopsy the pia over the base and convexities was infiltrated by white streaks. A large tumor was found in the right lateral ventricle arising in the thalamus. The neoplastic cells were round, with scanty cytoplasm. Some of the cells had long, thin processes. A diagnosis of primary glioma of the thalamus with subarachnoid metastases was made. Jacobi's [14] patient was a male infant of 1 year who had a history of three weeks of vomiting, drowsiness and convulsive movements. At autopsy a large cyst was found on the under surface of the right occipital lobe. In an article on primary sarcomatosis of the leptomeninges, Ford and Firor [15] recorded the case of a male infant of 15 months who had progressive bilateral cranial nerve palsy of six weeks' duration. At autopsy the base of the brain was covered by pinkish material which obscured the vessels and nerves. A tumor mass filled the fourth ventricle. The tumor had metastasized throughout the entire cerebrospinal fluid system and was present in the subarachnoid space over the posterior aspect of the spinal cord, in the ventricles and along the sheaths of the cranial nerves. The tumor was composed of irregular spindle-shaped cells with scanty cytoplasm and definite glia fibrils.

Derman's [16] case was that of an infant of 1 month whose head began to increase in size rapidly at the age of 2 days. A clinical diagnosis of internal hydrocephalus was made. At autopsy a large tumor was found in the pineal region. On microscopic examination it proved to be a teratoma. Bettinger's [17] patient was an infant of 20 months who had been in good health up to his sixteenth month, when he suddenly became ill with a high fever and twitchings of the left side of the body followed by drowsiness and rapid enlargement of the head. A clinical diagnosis of encephalitis was made. At postmortem examination the right ventricle was filled with a large tumor which was attached to the choroid plexus. It was a papilloma.

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13. Löwenberg, W.: Ueber die diffuse Ausbreitung von Gliomen in den weichen Häuten des Zentralnervensystems, Virchows Arch. f. path. Anat. **230**:99, 1921.

14. Jacobi, H. G.: A Case of Cerebral Cyst in an Infant, Am. J. Dis. Child. **25**:435 (June) 1923.

15. Ford and Firor: Primary "Sarcomatosis" of the Leptomeninges, Bull. Johns Hopkins Hosp. **35**:65, 1924.

16. Derman, G.: Zur Kenntnis der Teratome des Gehirns, Virchows Arch. f. path. Anat. **259**:767, 1925.

17. Bettinger, Hans: Zur Pathologie des Plexus chorioideus, Centralbl. f. allg. path. u. path Anat. **52**:321, 1931.

The purpose of this investigation was to determine the symptomatology, mode of development and histologic nature of tumors of the brain in infancy, and to indicate some of the diagnostic problems which differ from those presented by such tumors in later life. The study is limited to patients who were in their first or second year of life at the time of admission to the hospital, and is based on 9 examples of verified tumors of the brain in this age period. Tuberculomas and syphilomas were excluded. This study was limited to neoplasms primary in the brain or its coverings.

REPORT OF CASES

CASE 1.—H. K., a male infant of 16 months, had been well up to the age of 13 months, when he became irritable and suffered a gradual loss of the use of his upper extremities along with an enlargement of his head. On admission to St. Louis Children's Hospital examination showed a lethargic, hydrocephalic infant.

Fig. 1 (case 1).—Nodular tumor compressing the brain stem.

The optic disks were choked, the retinal veins engorged and the lower extremities spastic. A cerebellar craniotomy was done by Dr. Ernest Sachs. The basal cistern was filled with a large, lobulated tumor, but the precarious condition of the patient prohibited its removal, and the wound was closed, leaving a suboccipital decompression. Following this procedure the symptoms subsided for four months, when the head again began to enlarge. A second operation was performed, and the tumor partially removed, but the patient survived this procedure only two days. At autopsy the basal cistern was filled with a nodular tumor which extended along the base to envelop the brain stem and downward over the cervical cord (fig. 1). After hardening, the brain was cut. The tumor filled the fourth ventricle and invaded each cerebellar hemisphere (fig. 2).

Microscopic examination showed the tumor to be made up of cellular tissue of more or less uniform structure. The cells in some areas were arranged radially around the blood vessels. In other areas they formed true rosettes. The nuclei were oval; in each the chromatin formed several clusters. The histologic picture was characteristic of ependymoma (fig. 3).

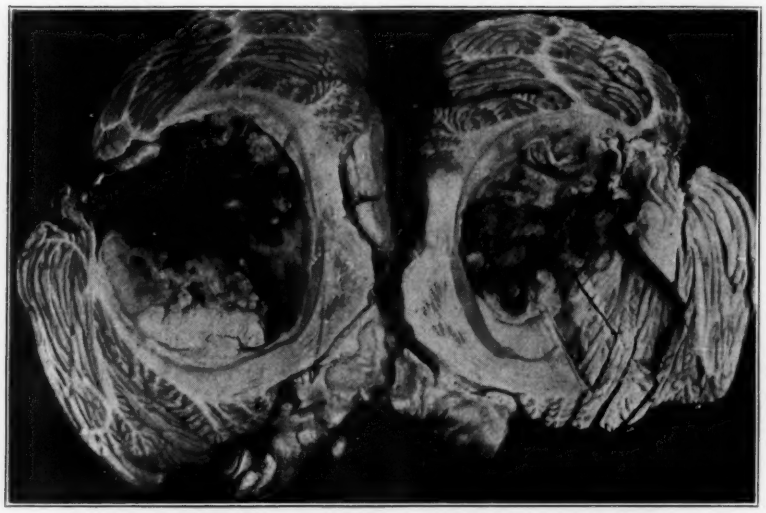

Fig. 2 (case 1).—Tumor invading each cerebellar hemisphere.

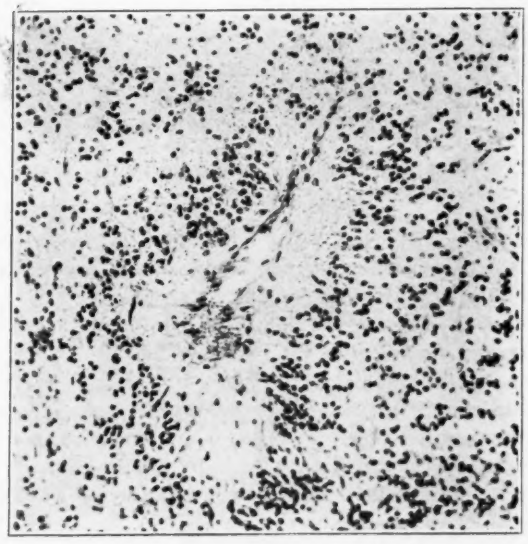

Fig. 3 (case 1).—Ependymoma. Hematoxylin and eosin; × 150.

Comment.—This case was previously reported by Fincher and Coon [18] in their article on ependymomas. As with other patients in this series the symptoms became manifest with the onset of hydrocephalus, as revealed by the rapid enlargement of the head.

CASE 2.—J. S., a male infant of 2 months was said to have been in good health up to two days before admission to the St. Louis Children's Hospital, when his head suddenly began to enlarge until at the end of forty-eight hours it had increased tremendously in size. Vomiting was the only other symptom noted by the parents. Examination showed an apathetic infant who was markedly hydrocephalic. The head measured 52 cm. in its greatest circumference, the fontanels were widened and tense and the veins of the scalp were dilated. Examination of the fundus revealed pale disks with engorged retinal veins. There were no paralyses and no other significant findings. Combined ventricular and spinal punctures showed free communication between the ventricles and the spinal subarachnoid space. The clinical impression was that of communicating hydrocephalus. A choroid-plexectomy was done by Dr. Ernest Sachs. The infant did well after this procedure, and was sent home three weeks later. At home he improved for two weeks, when he suddenly began to vomit and his temperature was elevated. He returned to the hospital in an extremely poor condition. The temperature was 40.5 C. (104.9 F.), the fontanels were sunken, and there was other marked evidence of dehydration. After a few days, following the free administration of fluids, the infant improved, and his temperature became normal. However, he continued to vomit and once more his head began to enlarge. A choroid-plexectomy was done on the other side, but the infant died. At autopsy a huge tumor was found arising in the pineal region. It extended backward into the midcerebellar region and compressed and distorted the entire brain stem. The tentorium was pushed upward by the growth, compressing both occipital lobes. The fourth ventricle was obliterated. The third ventricle and the anterior parts of both lateral ventricles were markedly enlarged (fig. 4).

The material had all been fixed in a dilute solution of formaldehyde, which limited the methods used in histologic study. Sections stained with hematoxylin and eosin showed cellular tissue. The cells were arranged in columns and around the blood vessels radially to form pseudorosettes. Two distinct types of nuclei could be distinguished among the tumor cells. The type predominating was large and vesicular, with a prominent nucleolus and scattered granules of chromatin. Here and there, irregularly distributed, were groups of deeply stained, small nuclei (fig. 5 *A*). Throughout the tissue was a fine connective tissue stroma which was stained salmon color by Davidoff's modification of Mallory's phosphotungstic acid and hematoxylin method. Glia fibrils were not found. The connective tissue was best shown by Perdrau's method of silver impregnation (fig. 5 *B*). Specific metallic impregnation for glia cells gave negative results. The pineal body was enlarged, and on section it was found to be made up of cells which could not be distinguished from tumor cells. The histologic diagnosis was pineoblastoma.

Comment.—The finding of a tumor of the brain was a great surprise. Bilateral choroid-plexectomies had been done for supposed communicating hydrocephalus, as demonstrated by double punctures before the first operation. It is to be regretted that the double puncture was not repeated before the second choroid-plexectomy, for it would undoubtedly have revealed obstructive hydrocephalus. Clinically, the picture seemed clearly one of hydrocephalus; however, with the information gained

18. Fincher and Coon: Ependymomas, Arch. Neurol. & Psychiat. **22**:19 (July) 1929.

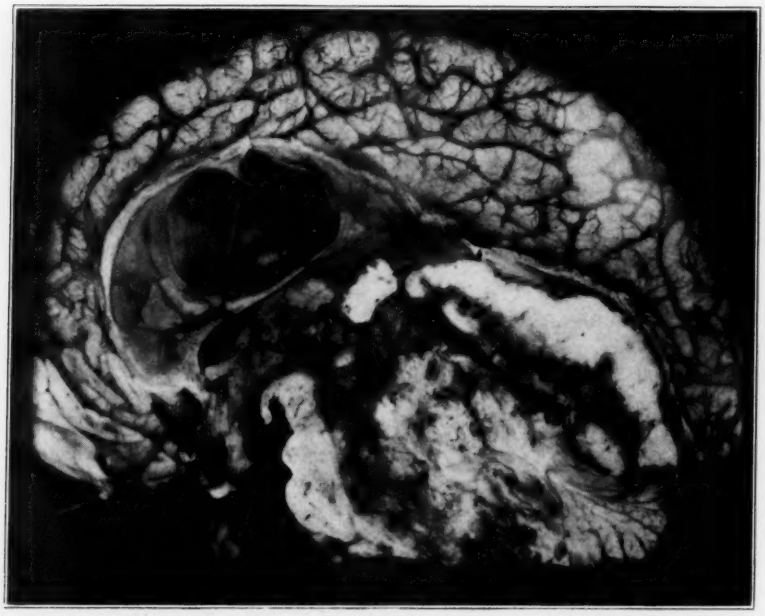

Fig. 4 (case 2).—Pineal tumor extending into the midcerebellar region.

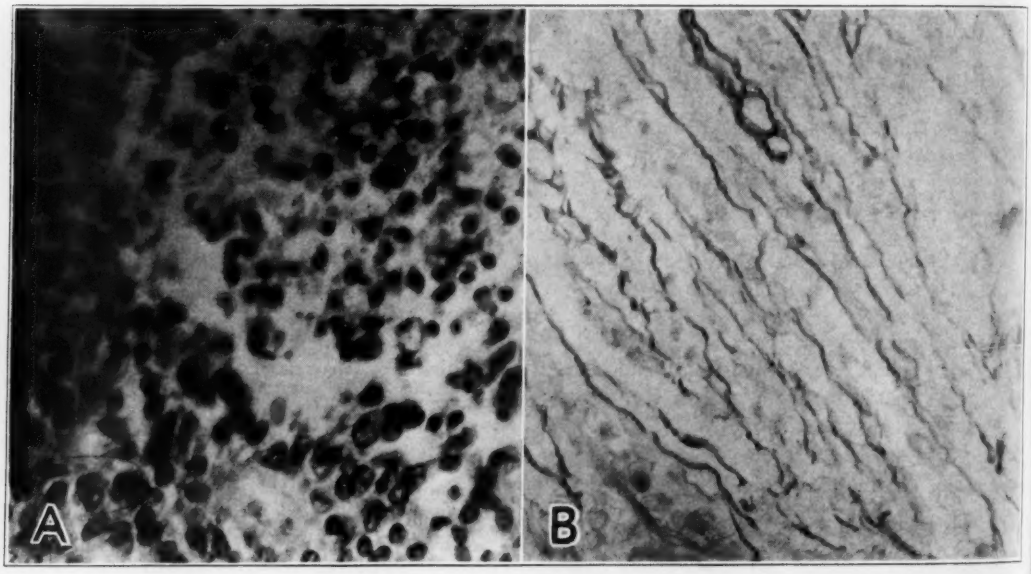

Fig. 5 (case 2).—*A*, pineoblastoma, showing the two types of nuclei. Hematoxylin and eosin; × 600. *B*, connective tissue stroma. Perdrau's method; × 150.

by this study, the abruptness of the onset and the rapid and enormous enlargement of the head were not in keeping with this diagnosis, and would seem to indicate that there had been a rather sudden obstruction to the circulation of the cerebrospinal fluid, as might have occurred when the tumor became of sufficient size to occlude the aqueduct of Sylvius.

From a surgical standpoint tumors in the pineal region are perhaps the least accessible, there being only a few examples in the literature of their successful removal. Microscopically the tumor was similar in structure to the pineal body of a fetus of 7½ months, as described by Globus and Silbert.[19]

Case 3.—G. T., a male infant of 20 months, had been in good health up to two months prior to admission to the St. Louis Children's Hospital, when he became irritable and had frequent attacks of vomiting; weakness of the entire right side developed and he lost his recently acquired ability to talk. On examination the patient was lethargic, responding only to painful stimuli. The fontanels were open and tense, the cranial sutures were separated, and percussion of the skull gave a cracked pot sound. The head was only slightly enlarged. Examination of the fundus revealed that the margins of both disks were blurred and the retinal veins engorged and tortuous. There was paresis of the right abducens muscle, central facial weakness on the right side and right hemiplegia. The clinical impression was of an expanding lesion in the left hemisphere, probably in the temporal lobe. An exploratory operation for an abscess was done through a trephine opening over the left temporal lobe. Yellow, clotting fluid was obtained, indicating a cystic tumor, so a large osteoplastic bone flap was made on the left side. This disclosed a large tumor which invaded the left hemisphere extensively. The tissue was removed for study and the wound closed, leaving a generous decompression. The child did poorly and died several days later.

The material removed at operation was fixed in Zenker's fluid, a solution of formaldehyde and ammonium bromide, and a dilute solution of formaldehyde. Microscopic examination showed the tumor to be extremely vascular. Areas of hemorrhage and necrosis were present throughout. The tissue was cellular, and the cells varied somewhat in size and shape. The nuclei were large and vesicular, each with a prominent nucleolus. The cytoplasm was finely granular, and even in the hematoxylin and eosin sections protoplasmic processes could be seen. Mitotic figures were present in moderate numbers. Many of the blood vessels showed hypertrophy of their walls, with marked intimal proliferation. In many areas the tumor cells were arranged around blood vessels and were attached to their walls by short stubby processes (fig. 6 *A*).

The cell processes were best shown by Hortega's silver carbonate method (fig. 6 *B*). In gold sublimate preparations (Cajal) the cells and cell processes could be demonstrated, but the results were not satisfactory. Perdrau's method of impregnation showed a marked hypertrophy of the connective tissue around the vessel walls (fig. 6 *C*). The histologic diagnosis was astroblastoma.

Comment.—Clinically, this case presented the picture of a rapidly expanding lesion in the left cerebral hemisphere, and a cystic tumor was disclosed at operation. The microscopic picture corresponded closely with that described by Bailey and Bucy [20] in their report of 25 cases of astroblastomas. In this case the demonstration of many astroblasts in the tumor, especially by Hortega's methods of

19. Globus and Silbert: Pinealomas, Arch. Neurol. & Psychiat. **25**:937 (May) 1931.

20. Bailey and Bucy: Astroblastomas of the Brain, Acta psychiat. et neurol. **5**:439, 1930.

silver impregnation, the large number of blood vessels with hypertrophied walls and the intervascular degeneration left little doubt as to the type of glioma. In the series reported by Bailey and Bucy [20] the youngest patient was 6 years old.

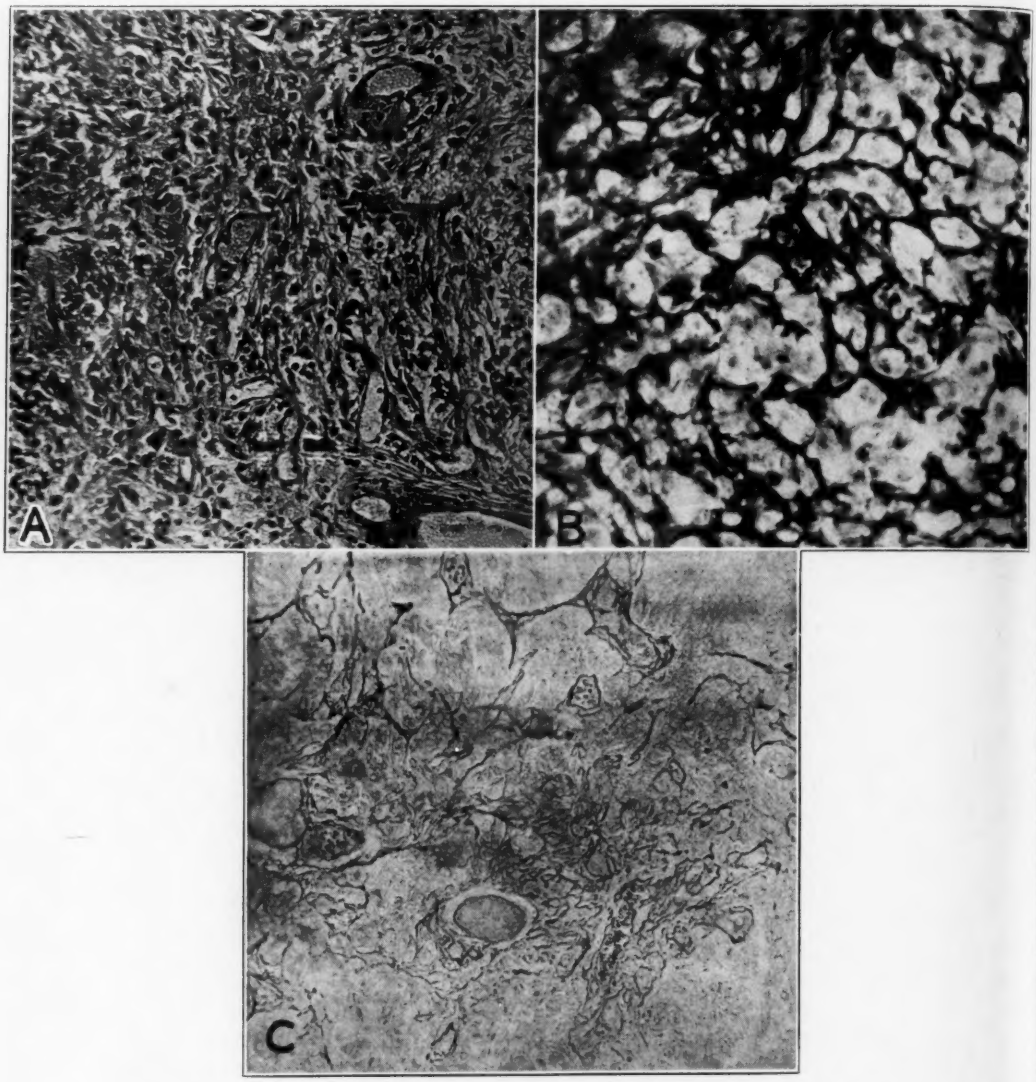

Fig. 6 (case 3).—*A*, astroblastoma. Hematoxylin and eosin; × 150. *B*, astroblasts. Hortega's silver carbonate; × 600. *C*, hypertrophy of the connective tissue around the walls of the vessels. Perdrau's method; × 150.

CASE 4.—H. J., a male infant of 14 months, was normal up to the age of 11 months, when he suddenly became "cross-eyed." This was followed shortly by fretfulness and severe constipation. Just before admission to the St. Louis Chil-

dren's Hospital peripheral facial weakness developed on the left side. On examination the patient was apathetic, but irritable when disturbed. The fontanels were open and tense and the head was retracted. The right pupil was larger than the left; both optic disks showed blurring of the margins, and the retinal veins were engorged. The infant had hemiparesis on the left, and the left side of the face was involved in its upper and lower branches, so that the left eye was held open all the time. A ventriculogram done the day following admission revealed bilaterally dilated ventricles. A cerebellar craniotomy was done by Dr. Ernest Sachs. A large midline cystic tumor was disclosed. The mural nodule and part of the wall of the cyst were removed. The infant made a prompt recovery, and when last seen one month later in the outpatient department he was in good health. Subsequent attempts to reach the parents of the child by follow-up letters were unsuccessful.

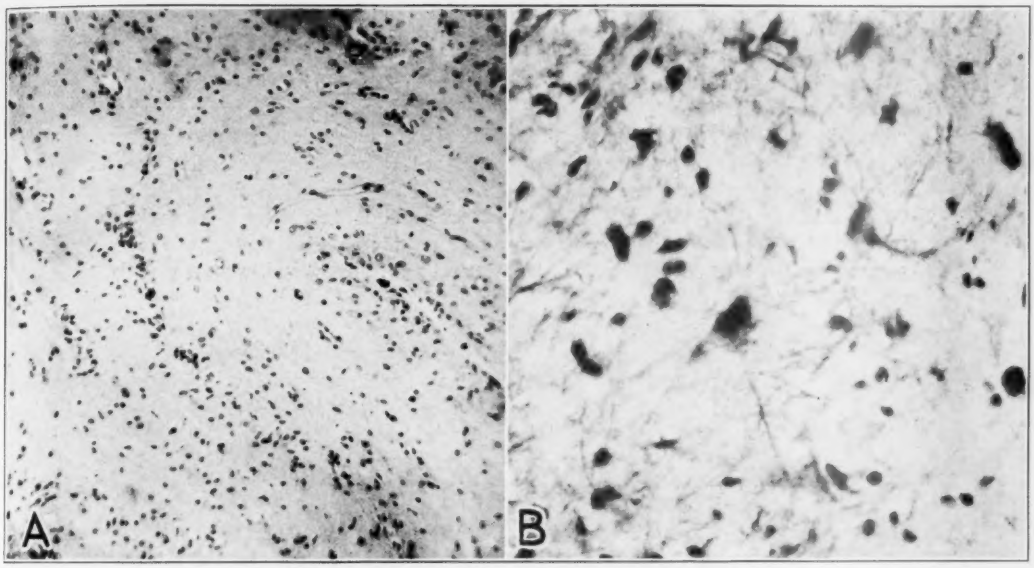

Fig. 7 (case 4).—*A*, astrocytoma. Hematoxylin and eosin; × 150. *B*, astrocytes. Gold sublimate method of Cajal; × 600.

Microscopic examination of the tumor removed at operation showed a tissue which was more or less uniform in structure. The nuclei were scattered evenly throughout the field. There were a moderate number of thin-walled blood vessels (fig. 7 *A*). Many well differentiated neuroglial fibers could be demonstrated with Mallory's phosphotungstic acid and hematoxylin stain. By Cajal's gold sublimate method many astrocytes with long, tenuous processes were impregnated (fig. 7 *B*). The histologic diagnosis was astrocytoma.

Comment.—The clinical picture in this case, as in others in this series, would not permit of a pathologic or localizing diagnosis. The presence of dilated ventricles demonstrated by ventriculography led to an exploration of the posterior fossa and the removal of the mural nodule from the midline cystic astrocytoma. The importance of the removal of the mural nodule in order to insure a long survival has been emphasized by Cushing, who recently reported a series of 76 cere-

bellar astrocytomas.[21] In his series only 2 patients were under 2 years of age, one being 22 months and the other 23 months old.

CASE 5.—B. B., a male infant of 23 months, was admitted to the St. Louis Children's Hospital because of inability to walk and an increase in the size of the head. He was said to have been normal at birth and in good health up to his seventeenth month, when, after a febrile illness of short duration, there was a noticeable alteration in his gait, which became awkward and unsteady. The disturbance in gait became progressively worse, and after a few weeks he was no longer able to walk. At this time there was a marked change in his disposition. The previously well behaved and placid child became fretful and irritable. He had frequent bouts of vomiting, and his head became markedly enlarged. On admission to the hospital the infant's head measured 54.5 cm. in its greatest circumference, and was kept turned to the right. The fontanels were widened and bulging. The margins of the optic disks were slightly hazy and the retinal veins engorged. The deep reflexes in the lower extremities were hyperactive, there was a bilateral ankle clonus, and, on plantar stimulation, dorsiflexion of both great toes. Clinically, a diagnosis of postinflammatory obstructive hydrocephalus was made. The morning after admission the child had a bout of severe vomiting, becoming cyanotic and suddenly died. At the postmortem examination a huge, firm, white neoplasm was found on the under surface of the left cerebellar hemisphere, extending anteriorly and compressing the pons and medulla. After hardening in a dilute solution of formaldehyde, U. S. P. (1:10), the brain was sectioned in the median sagittal plane and the huge solid tumor was seen filling the fourth ventricle and markedly compressing the cerebellum (fig. 8). The lateral and third ventricle were greatly enlarged.

Microscopic examination showed the tumor to be composed of moderately cellular tissue, in which the cells were arranged radially around the numerous blood vessels (fig. 9*A*). Around each blood vessel was a clear space, which, in the phosphotungstic acid and hematoxylin stained sections, was filled in with cell processes. Two types of cells could be differentiated in the preparations. The predominant cell type was columnar, with a small, round, deeply stained nucleus. Scattered irregularly in the tissues were polygonal cells with large vesicular nuclei and spiny cytoplasmic processes. These processes were best demonstrated in the sections stained with gold sublimate, which also impregnated many cells each with a long, sturdy process attached to the wall of a blood vessel (fig. 9*B*). The histologic diagnosis was ependymoma.

Comment.—This infant was in the hospital twenty-four hours when it suddenly died, before the clinical investigation could be completed. Because of the febrile disease which just preceded the appearance of symptoms indicative of an intracranial disease, a tentative diagnosis of postinflammatory obstructive hydrocephalus was made. The huge tumor in the fourth ventricle found at postmortem examination was very firm. It extended into the basal cistern and spread along the base so as to compress the brain stem. The midcerebellar region is a favorite site for tumors of the brain, especially in childhood. Medulloblastomas and cerebellar astrocytomas are found most frequently in this region. In Cushing's series of over 2,000 verified tumors of the brain [22] there were 25 ependymomas, of which 19 were

21. Cushing, Harvey: Experiences with the Cerebellar Astrocytomas, Surg., Gynec. & Obst., **52**:129, 1931.

22. Cushing, Harvey: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

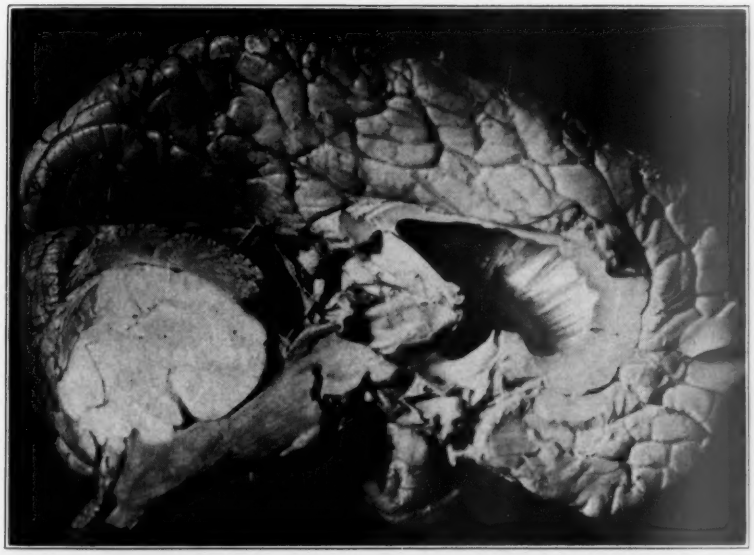

Fig. 8 (case 5).—Ependymoma in the fourth ventricle.

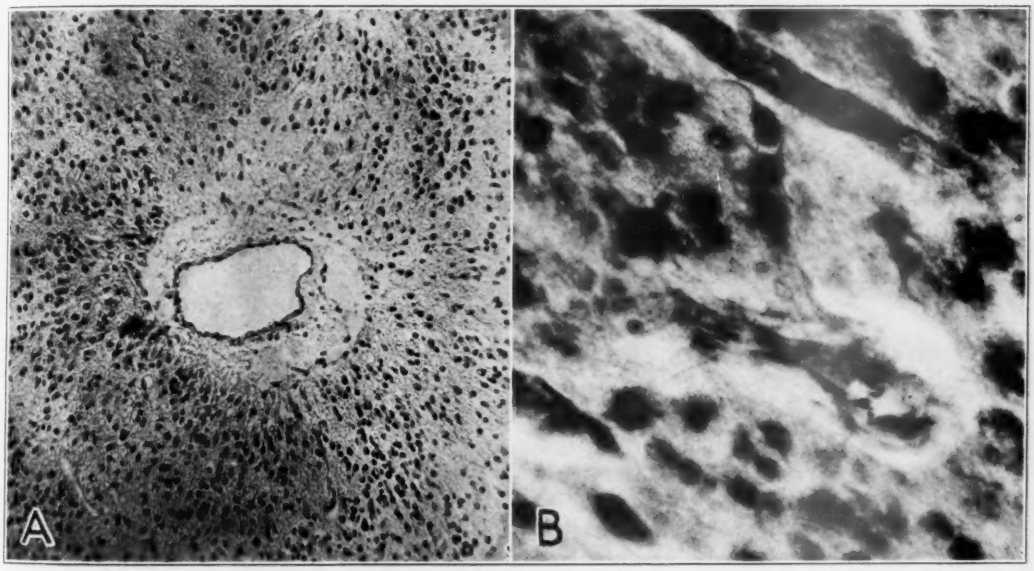

Fig. 9 (case 5).—*A*, ependymoma showing radial arrangement of the cells around the blood vessels. Hematoxylin and eosin; × 150. *B*, cell processes attached to walls of the vessels. Gold sublimate method of Cajal; × 600.

disclosed in the course of explorations for midcerebellar tumors. Canavan and Hemsath [23] recently described a small body made up of ependymal cells in the floor of the fourth ventricle of an infant prematurely born who died a few hours after birth.

CASE 6.—J. C., a male infant of 19 months, had been in good health up to one month prior to admission to the St. Louis Children's Hospital, when he suffered a minor injury to his head. This was followed by vomiting and an abnormal attitude of the head, which was held tilted toward the left shoulder. There was a marked change in his disposition. The previously alert and placid infant became apathetic

Fig. 10 (case 6).—Ventriculogram showing dilated ventricles.

and fretful when disturbed. Examination showed the infant's head to be enlarged, measuring 54 cm. at the greatest circumference. Both optic disks were choked, and the retinal vessels were engorged and tortuous. Both lower extremities were spastic. Ventriculography revealed bilaterally dilated ventricles (fig. 10). Cerebellar exploration was undertaken by Dr. Sachs. The infant's condition became very poor while on the table; so it was necessary to conclude the operation without attempting to locate the tumor. The dura was left open, and a large decompression made. The patient did not rally from the operation, and after a few days died

23. Canavan, M. M., and Hemsath, F. A.: Glioma in the Fourth Ventricle of a Prematurely Born Infant, Arch. Neurol. & Psychiat. **26**:1234 (Dec.) 1931.

of pneumonia. At the autopsy a large, soft tumor filled the fourth ventricle. The lateral and third ventricles were greatly dilated.

At the time of microscopic examination the material had been in a dilute solution of formaldehyde for more than five years. The tumor was extremely vascular and of more or less uniform structure throughout. The cells were for the most part irregularly displaced, though there was a tendency to the formation of rosettes. The tissue was permeated by a fine capillary network. The nuclei of the tumor cells were small, round and deeply stained, in contrast to those of the walls of the vessels which were large, vesicular and pale (fig. 11 *A*). The neoplastic cells had a thin rim of lightly stained cytoplasm, which in many of the cells tapered off at one pole, giving the cell a carrot-shaped appearance. Numerous mitoses were present. With Mallory's phosphotungstic acid and hematoxylin stain

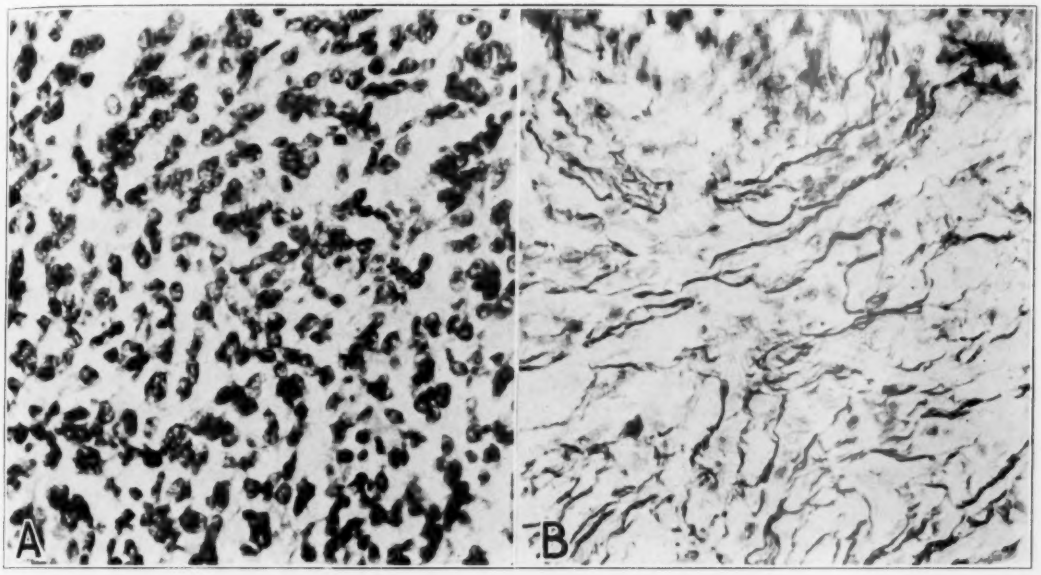

Fig. 11 (case 6).—*A*, medulloblastoma. Hematoxylin and eosin; × 600. *B*, connective tissue around the walls of the vessels. Perdrau's method; ×150.

glia fibrils could be demonstrated. The connective tissue was differentially stained salmon by this method. Silver impregnation (Perdrau) showed the connective tissue distributed around the capillary walls (fig. 11 *B*). The histologic diagnosis was medulloblastoma.

Comment.—In this case the onset of symptoms followed a minor injury of the head. The disease ran a rapid course. One month after its appearance, at the time of admission to the hospital, the infant was failing rapidly, and died shortly after a cerebellar decompression. Histologically the tumor was cellular with abundant mitoses, and was classified as a medulloblastoma, a group of gliomas, the most frequent site of which is the midcerebellar region in children. These tumors were formerly described as small round cell sarcomas. However, the demonstration of glia fibrils by Mallory's stain and the distribution of the connective tissue around

the vessel walls, as shown by Perdrau's method, clearly differentiate this group from the sarcomas, whether primary in the brain or metastatic.

CASE 7.—G. S., a female infant of 17 months, had been in good health up to the age of 15 months, when, following a mild infection of the upper respiratory tract, she began to vomit. She soon lost her recently acquired ability to walk, and her head began to enlarge rapidly. On admission to the St. Louis Children's Hospital examination revealed an apathetic infant with the head enormously enlarged; the fontanels open and bulging and a left internal squint. The margins of both optic disks were blurred, and the retinal veins engorged. A double puncture (one needle in the lateral ventricle and the other in the spinal subarachnoid space) revealed obstructive hydrocephalus. A cerebellar exploration was performed by Dr. Sachs, and a large midline tumor was found and partially removed.

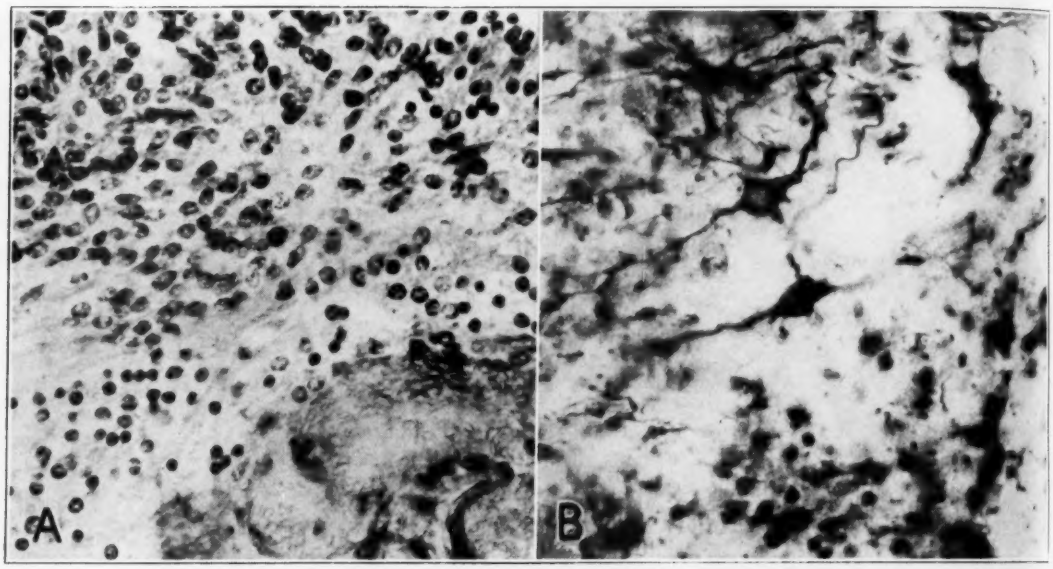

Fig. 12 (case 7).—*A*, medulloblastoma. Hematoxylin and eosin; × 450. *B*, spongioblasts in the medulloblastoma. Hortega's silver carbonate method; × 600.

Following the operation the infant was given roentgen therapy; however, her condition never improved, and she died six months after the operation. At autopsy the muscles and connective tissue at the site of the cerebellar craniotomy were invaded by a tumor. The cisterna magna and fourth ventricle were filled with a large mass. The arachnoid space over the frontal lobes was infiltrated by the tumor. There was marked dilatation of the lateral and third ventricles.

On microscopic examination the tissue removed at operation was quite cellular. There were numerous vessels throughout. The walls of the vessels were markedly thickened by an overgrowth of the connective tissue. The tumor cells were more or less uniform in size and shape. Their nuclei were round, each with a prominent nucleolus. The cytoplasm was scanty and pale staining, forming a thin rim around the nucleus (fig. 12 *A*). There was considerable old hemorrhage in the tumor. Numerous spongioblasts were impregnated by Hortega's silver carbonate

method (fig. 12 *B*). An occasional astrocyte was found in the gold sublimate preparations (Cajal). The histologic diagnosis was medulloblastoma.

Comment.—The onset of symptoms of increased intracranial pressure followed a mild infection of the upper respiratory tract. As in many cases of tumor of the brain in children vomiting was one of the early symptoms, and the physicians under whose care the infant first came focused their attentions on the gastro-intestinal tract. Not until rapid enlargement of the head became manifest did they suspect the intracranial cavity as the source of the symptoms and seek neurosurgical aid. At the time of the operation there was an extreme degree of hydrocephalus, and no improvement followed the partial removal of the tumor and roentgen therapy. The presence of tumor nodules in the arachnoid space over the frontal lobes emphasized the method of dissemination of the neoplastic cells through the cerebrospinal fluid spaces. This occurred in spite of thorough irradiation which was instituted after the operation.

CASE 8.—B. F., a male infant of 16 months, was in good health up to six weeks before admission to the University of Chicago Clinics, when he began to have frequent attacks of vomiting. He became lethargic, and a right internal squint developed. Examination revealed an apathetic, hydrocephalic infant. Both optic disks were choked, and the pupils were dilated and failed to react to light. Irregular twitchings were present in the extremities. The deep reflexes were all hyperactive. A ventriculogram was made (Dr. Paul Bucy). The patient was very feeble and died a few hours later. The ventriculogram showed marked internal hydrocephalus. The third ventricle was partially filled, but the fourth ventricle was not visualized. At autopsy the brain was greatly enlarged and the convolutions flattened. On the inferior surface of the right cerebellar hemisphere a soft, pinkish-white tumor was attached to the leptomeninges, but not to the dura (fig. 13). After hardening in a dilute solution of formaldehyde the brain was cut in the midsagittal plane. The tumor was in the fourth ventricle extending into the right cerebellar hemisphere (fig. 14). There were marked widening and thinning of the floor of the third ventricle, which was ballooned downward posterior to the optic chiasm. The tumor in the fourth ventricle extended forward into the posterior meatus of the aqueduct of Sylvius.

On microscopic examination the tumor was quite cellular. The cells for the most part were spindle-shaped, and were arranged radially around the numerous blood vessels. The nuclei were small and round, with scattered granules of chromatin. Surrounding each vessel was an area free from nuclei (fig. 15 *A*). With Mallory's phosphotungstic acid and hematoxylin stain the area around each vessel was seen to contain cell processes (fig. 15 *B*). The histologic diagnosis was ependymoma.

Comment.—The sudden onset of symptoms and their rapid development were no doubt the result of the occlusion of the posterior meatus of the aqueduct of Sylvius by the tumor.

CASE 9.—A. W., a male infant of 11 months, began to have convulsions soon after birth. After the second week he seemed well; he gained weight and developed normally until the age of 10 months, when the mother noticed that his head was rapidly increasing in size. The infant became drowsy, and had frequent spells of vomiting. In this condition he was admitted to the University of Chicago Clinics. The patient was lethargic, responding only to painful stimuli; the head was enormously enlarged, and the fontanels were tense and bulging. The pupils were dilated and reacted to light sluggishly. The fundi were normal and the

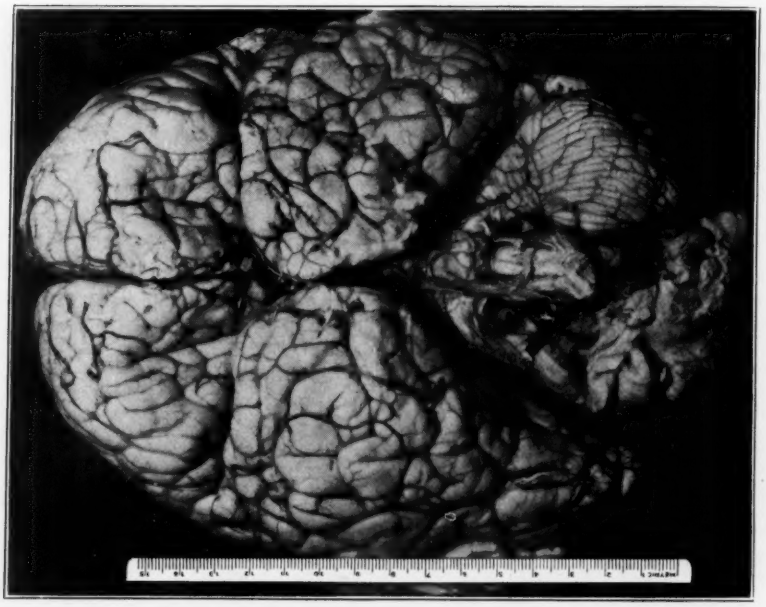

Fig. 13 (case 8).—Tumor on the inferior surface of the right cerebellar hemisphere.

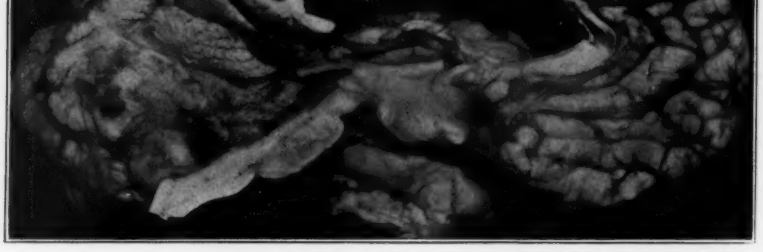

Fig. 14 (case 8).—Midsagittal section showing tumor in the fourth ventricle.

ocular movements unimpaired. The extremities were spastic, and Babinski's sign was present on both sides.

The patient declined rapidly and grew deeply comatose. Trephine openings were made over both temporal lobes (Dr. Paul Bucy) in search of a subdural hematoma, which, however, was not found. The infant became progressively worse and died two days later. At autopsy many soft, white nodules were present everywhere in the subarachnoid space of the brain and spinal cord (fig. 16). It was impossible to determine where the neoplasm had its origin. After removing specimens of fresh tissue for special fixation, the brain and spinal cord were hardened in a solution of formaldehyde. When the brain was cut, nodules of the tumor were found in the fourth and lateral ventricles. There was marked internal hydrocephalus.

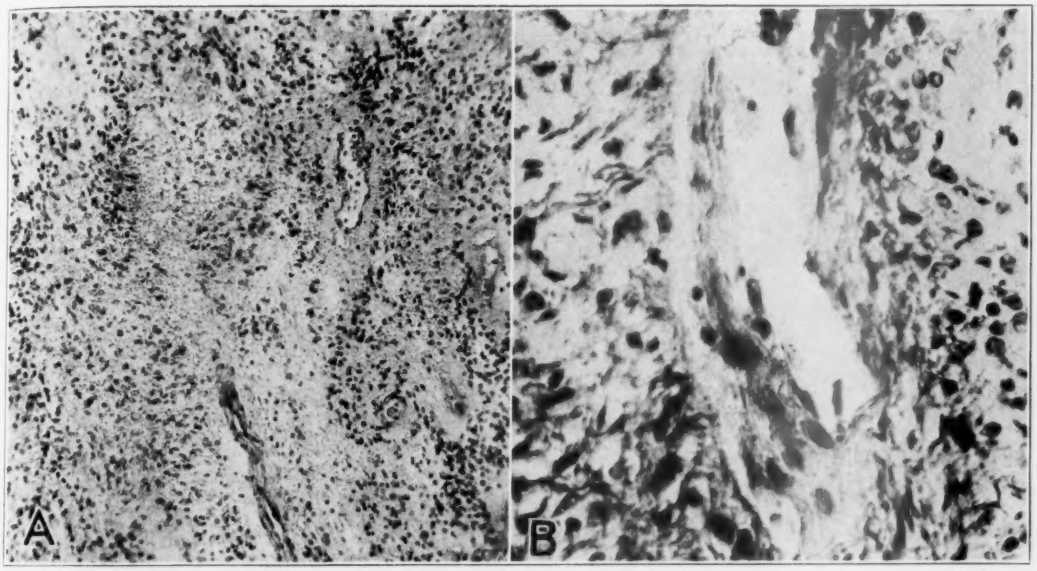

Fig. 15 (case 8).—*A*, ependymoma. Hematoxylin and eosin; × 80. *B*, cell processes around the vessel wall. Mallory's phosphotungstic acid and hematoxylin; × 600.

Tissue fixed in Zenker fluid was stained with hematoxylin and eosin. The tumor had no capsule; it invaded the brain tissue by infiltration along the blood vessels. The nuclei in the cells of the walls of the blood vessel were distinct from those of the tumor cells. There was a certain amount of connective tissue stroma which divided the tumor cells into masses in an alveolar fashion. In the neoplastic cells were a great number of pyknotic masses that were interpreted as abnormal and degenerating mitoses. The nuclei of the tumor cells were oval, with prominent nucleoli. They were about the same size as the neuroglial nuclei in the adjacent brain tissue. The cells had scanty, lightly stained cytoplasm and lay in loose masses without any particular arrangement. In some areas swarms of mitoses were easily recognized (fig. 17 *A*).

Silver impregnation (Perdrau) of material fixed in a dilute solution of formaldehyde showed scattered small, thin-walled blood vessels, with strands running between them and dividing the tumor cells into masses which contained no reticulin (fig. 17 *B*). With Mallory's phosphotungstic acid and hematoxylin stain the connective tissue stroma was clearly differentiated, stained salmon. The tumor cells did not form differentiated neuroglial fibers. Nissl preparations of material fixed

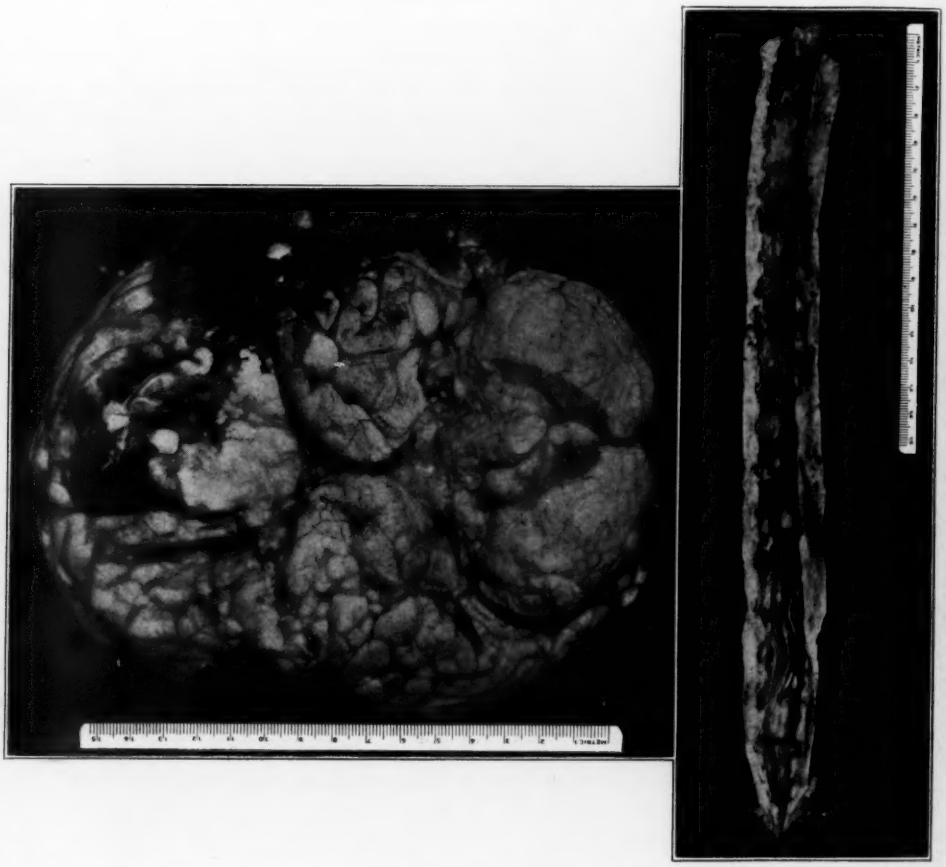

Fig. 16 (case 9).—Brain and spinal cord showing nodules of the tumor widely disseminated in the subarachnoid space.

in alcohol showed the tigroid substance in the adjacent brain sharply stained. No Nissl substance was found in the tumor cells.

After fixation in a solution of formaldehyde and ammonium bromide silver impregnation was done. Hortega's silver carbonate method, Penfield's combined method for microglia and oligodendroglia and Rydberg's silver-diamino carbonate method [24] were employed. The last mentioned method gave the sharpest impregnation, and many cells with short processes were demonstrated (fig. 17 *C*).

24. Rydberg, Eric: Cerebral Injury in New-Born Children Consequent on Birth Trauma, Acta path. et microbiol. Scandinav., supp. 10, 1932, p. 1.

Of the same tissue gold sublimate preparations were made. In these one saw cells which were impregnated in a granular fashion in the neighborhood of blood vessels. These cells had a small amount of cytoplasm around the nucleus and a few tenuous processes. They resembled the perivascular astrocytes of Andriezen

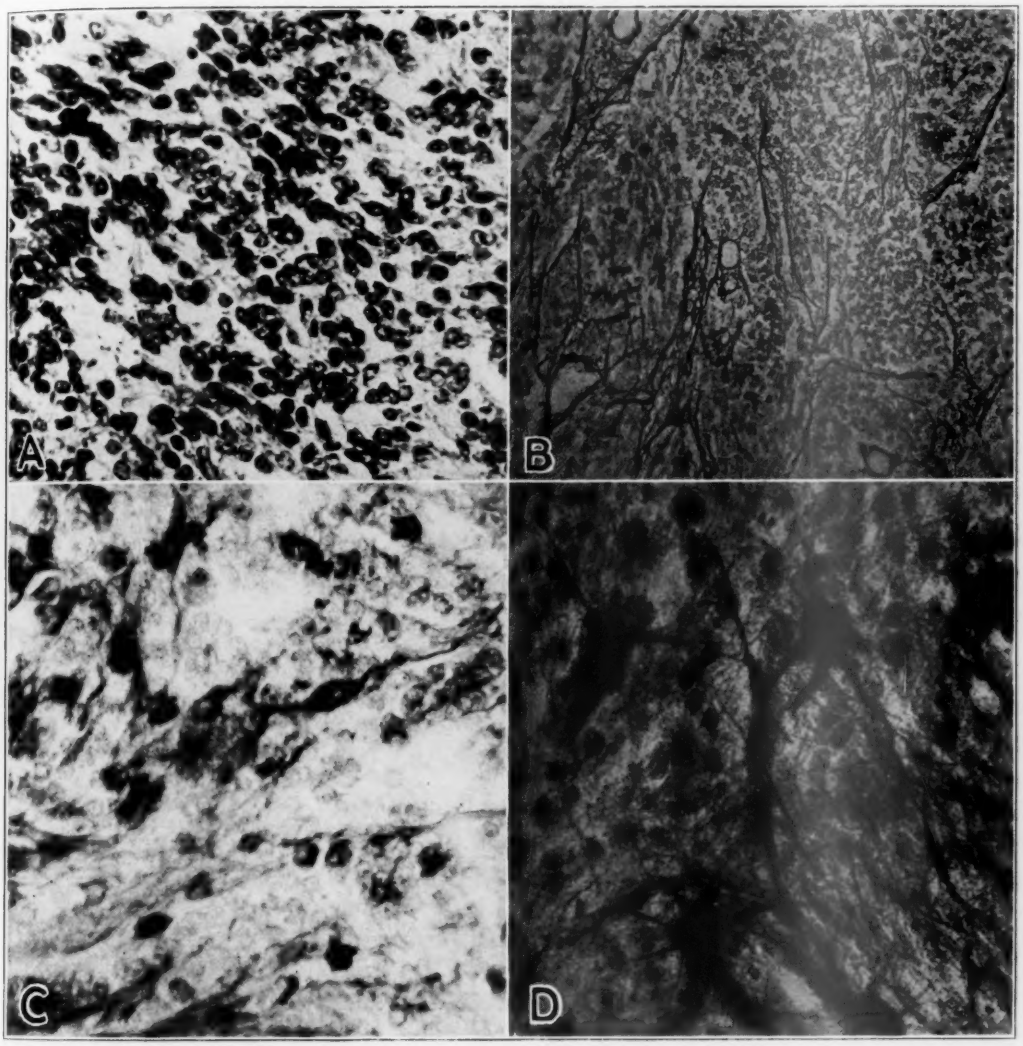

Fig. 17 (case 9).—*A*, the irregular arrangement of the tumor cells. Iron and hematoxylin; × 600. *B*, distribution of the connective tissue around the blood vessels. Perdrau's method; × 150. *C*, cells of glial origin, Rydberg's silver-diamino carbonate method; × 600. *D*, astrocytes. Gold sublimate method of Cajal; × 600.

(fig. 17 *D*). Fat stain (Herxheimer) showed a considerable amount of degeneration throughout the tissue. Best's carmine stain demonstrated small granules of

glycogen in many of the cells. Nerve fibers were not found in the tumor tissue by the method of either Cajal or Ranson. The tumor tissue in the subarachnoid space surrounding the spinal cord was similar to that previously described (fig. 18).

Comment.—This is an example of a tumor of neuro-epithelial origin which metastasized widely throughout the subarachnoid space and ventricles. Histologically the tumor resembled the gliomas of the fourth ventricle of children described by Bailey and Cushing,[25] and called by them medulloblastomas. In the 61 cases reported by Cushing, in 1930,[26] the youngest patient was 2 years old. The tendency of medulloblastomas to become disseminated throughout the cerebrospinal fluid system is well known to neurosurgeons and neuropathologists. In

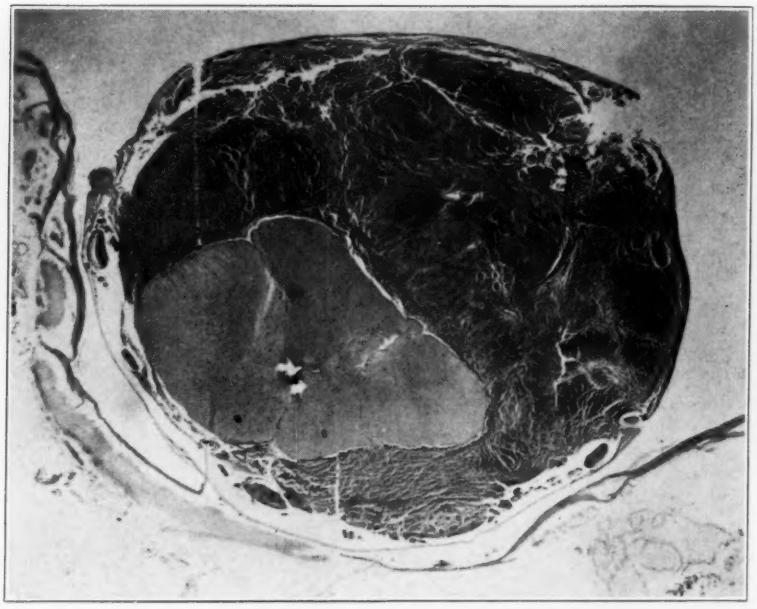

Fig. 18 (case 9).—Tumor tissue in the subarachnoid space surrounding the spinal cord.

this case the metastases were extensive and widespread in the central nervous system, so that it was impossible to determine the location of the primary neoplasm. From a histologic standpoint the tumor presented difficulties in classification. The individual cells resembled those seen in medulloblastomas, but there was no tendency to the formation of rosettes. By Rydberg's silver-diamino carbonate method many cells with short processes could be demonstrated. These could not be identified with certainty by any other method, but were, no doubt, undifferen-

25. Bailey and Cushing: Medulloblastoma Cerebelli: A Common Type of Midcerebellar Glioma of Childhood, Arch. Neurol. & Psychiat. **14**:192 (Aug.) 1925.

26. Cushing, Harvey: Experiences with the Cerebellar Medulloblastomas, Acta path. et microbiol. Scandinav. **7**:1, 1930.

tiated glia cells. A few adult astrocytes were found in the Cajal gold sublimate preparations. The histologic diagnosis was embryonic tumor of neuro-epithelial origin, closely related to medulloblastomas.

COMMENT

A study of 9 cases of tumors of the brain in infants revealed several interesting observations. The preponderance of tumors of the brain in male infants is brought out in this small series, 8 of the 9 patients having been males. This corresponds with the observation of Wollstein and Bartlett [8] who found that 7 of their 9 cases in children under the age of 3 occurred in male patients. In the scattered reports in the literature of single cases of tumors of the brain in infancy the male sex predominates. Cushing,[26] in a series of 61 midcerebellar medulloblastomas, found them to be three times more common in males than in females.

Hydrocephalus was present in every case in this series. In 7 it was the most prominent feature, overshadowing other findings so much that bilateral choroid-plexectomies were done in 1 case in which an unsuspected pineal tumor was discovered at autopsy. Rapid enlargement of the head was observed by the parents in 7 cases, and in 2 it was the first symptom which aroused the suspicion that an abnormality existed. Vomiting was present in all but 2 cases and often misled the attending physicians into directing their attention to the gastro-intestinal tract. Choked disks were present in 5 patients; in 3 there was no elevation of the disks, but the retinal veins were engorged, and in 1 the fundi were described as normal.

The correct clinical diagnosis was suspected in only 3 cases. The other clinical diagnoses were: obstructive hydrocephalus, communicating hydrocephalus, abscess of the brain and subdural hematoma. Seven of the tumors were located in the midcerebellar region, 1 in the pineal region and 1 in the left cerebral hemisphere. The midcerebellar region as the site of tumors of the brain in early life was pointed out by Cushing in his articles on cerebellar astrocytomas [21] and medulloblastomas.[26] He ventured the opinion that the structurally complicated region of the tegmental plate of the fourth ventricle offers a choice opportunity for the occurrence of embryonic cell rests which subsequently undergo neoplastic proliferation. In this series were 3 ependymomas, 1 pineoblastoma, 1 astroblastoma, 1 astrocytoma, 2 medulloblastomas and 1 embryonic tumor of neuro-epithelial origin which could not be classified further. The ependymomas were all found in the fourth ventricle. They were all solid tumors, histologically similar to ependymomas described in other age periods. The pineoblastoma occurred in a very young infant, and corresponded in structure to the pineal gland of a fetus of 7½ months, as described by Globus and Silbert.[19] The single example of a tumor of the cerebral hemisphere in this series was an astroblastoma.

Bailey and Bucy [20] reported a series of 25 astroblastomas, all of which were in the cerebral hemispheres. The 1 case of astrocytoma reported here was unusual only because it occurred in an infant of 14 months. The 2 medulloblastomas presented the typical gross and histologic appearance of those described in later childhood. In 1 case (9) a tumor of neuro-epithelial origin could not be classified further. It presented many of the characterstics of medulloblastomas, including the tendency to metastasize through the entire cerebrospinal fluid system.

The difficulties encountered in the diagnosis of tumors of the brain in infancy have already been alluded to. Many of the signs on which one relies in the study of the diseases of the nervous system in later life are invalidated by the chaotic state of the conventional neurologic reflexes in infancy; hence, one is forced to depend more on the history and on observations of the general behavior of the infant. The marked enlargement of the head in 7 of the cases reported here and in many of those in the literature indicates that the problem of diagnosis resolves itself into a differentiation of hydrocephalus due to tumor from that due to other causes. Dandy [27] expressed the opinion that about two thirds of all cases of obstructive hydrocephalus were caused by stricture of the aqueduct of Sylvius. In such cases enlargement of the head is present at birth or occurs soon afterward. In the 9 cases of this series the head was said to have been of normal size at birth. One has been impressed by the sudden and rapid enlargement of a previously normal head in cases of tumor of the brain in the first two years of life. Ventriculography, which has proved of great value in the demonstration and localization of tumors of the brain in later life, is not as helpful in infancy. The presence of dilated lateral and third ventricles in the films merely indicates a failure of air to enter the fourth ventricle. This may be due to an obstruction of the aqueduct, to a tumor filling the fourth ventricle or to technical difficulties inherent in the procedure. However, the demonstration of a normal or enlarged fourth ventricle in the presence of dilated lateral and third ventricles indicates that the obstruction is caudal to the fourth ventricle at the formina of Magendie and Luschka, or that one is dealing with communicating hydrocephalus, due either to hyperactivity of the choroid plexuses or to a defect in the absorption of cerebrospinal fluid in the subarachnoid spaces.

Subdural hematomas occur much more frequently in infancy than has been realized in the past, and are often the cause of enlargement of the head. By careful taking of the history and clinical studies this condition can usually be differentiated from tumor of the brain. Subdural hematomas occur most frequently during the first year of life in

27. Dandy and Blackfan: Internal Hydrocephalus, Am. J. Dis. Child. **14**:424 (Dec.) 1917.

infants who are poorly nourished or rachitic or who have had a severe infectious disease. Convulsions and enlargement of the head were found by Sherwood [28] to be the two most constant symptoms. Hemorrhages in the eyegrounds were present in about half the cases. The bulging of the fontanels, which is an early sign in tumors of the brain, appears late in cases of subdural hematoma. Lumbar puncture may yield a clear fluid, as may ventricular puncture, but a needle introduced into the subdural space through the fontanel gives bloody or xanthochromic fluid.

Abscesses of the brain, though they occur, are very rare in infancy. The history of a discharging ear or a septic focus elsewhere in the body should suggest that the brain may harbor an abscess.

SUMMARY

1. Nine cases of tumor of the brain in infancy have been reported and the literature reviewed.

2. The differences between the intracranial changes produced by an expanding lesion in infancy and those produced in later life are due to the elasticity of the cranial bones in infancy which permit spontaneous decompression to occur as the lesion increases in size.

3. During early life tumors of the brain seem to be much more common in males than in females.

4. Enlargement of the head was a constant finding in 9 cases of tumor of the brain in infancy.

5. The midcerebellar region is the site of election of tumors of the brain in infancy, and was the location in 7 of the 9 cases reported here.

Histologically, neoplasms in infancy usually arise from glial elements and resemble the gliomas found in later life in similar locations.

7. Study of the literature indicates the occurrence of teratomas and sarcoma also in this age period.

8. In the differential diagnosis hydrocephalus due to causes other than tumor of the brain must be considered, notably, obstruction of the aqueduct, the result of either an inflammatory process or a congenital defect, communicating hydrocephalus, subdural hematoma and abscess of the brain.

Dr. Ernest Sachs permitted me to report cases 1 to 7 from his service and Dr. Percival Bailey, cases 8 and 9.

28. Sherwood, David: Chronic Subdural Hematoma, Am. J. Dis. Child. **39**: 980 (May) 1930.

ETIOLOGY OF MONGOLISM

WITH SPECIAL REFERENCE TO ITS OCCURRENCE IN TWINS

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AND

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LOS ANGELES

Cases of mongolism in twins are rather rare. We have been able to find reports of only 59 such cases in the literature. They are of special interest in that they afford an opportunity, not otherwise available, of investigating certain phases of the etiology of that condition.

In the course of a study of mental disorders in twins, undertaken over three years ago, we have collected records of 1,014 pairs of twins one or both of whom presented a mental disorder. The material is now being analyzed by clinical groups.

In our collection are included records of 5 pairs of twins with mongolism. The object of this communication is twofold: first, to report our cases, and second, to utilize this and other material in a study of the etiology of mongolism.

REPORT OF CASES

CASE 1.—*Monozygotic female twins, both affected.*

The T. twins, Florence and Frances, were born in Brookline, Mass., on March 24, 1924, being the last born of 6 children in the family. Labor was premature by six weeks. No information was available as to the conditions at birth, but the twins were judged to be monozygotic by reason of their close resemblance to each other in every respect. The mother stated that she confused them constantly; they cried at the same time and reacted in the same way in any situation; they cut their first teeth on the same day, at the age of 16 months; together they went through attacks of colds, discharging ears, bronchopneumonia, lobar pneumonia and whooping cough.

On Oct. 25, 1928, they were examined at the Walter E. Fernald School at Waverley, Mass.; both were found to present typical mongolism and showed, on tests, intelligence quotients of 44 and 40, respectively. On Sept. 18, 1929, they were admitted to the State School at Wrentham, Mass. There, too, their close resemblance to each other was noted; they were found to be alike as to features, color of skin, color and texture of hair, and teeth; each was found to have a congenital cardiac lesion. Intelligence tests administered at the Wrentham school on Dec. 31, 1929, revealed an intelligence quotient of 30 for each.

Early in January 1930, acute bronchitis developed in both twins, and on January 12 Frances died. On being notified, the mother said: "Then Florence will be dead in a week's time." The physicians at the institution made a special effort to prevent this, but in spite of it Florence died on January 22.

CASE 2.—*Dizygotic female twins, one affected.*

The H. twins, Margaret and Mildred, were born in Wakefield, Mass., on July 14, 1909. Both parents were 25 years of age when the twins were born. There were 2 children older and 1 child younger than the twins, all normal. The birth of the twins was at full term. Margaret weighed 8 pounds (3,629 Gm.) and Mildred 9 pounds (4,082 Gm.). It was specially noted that there were two after-births, as the physician in attendance went away and was called again to deliver the second after-birth. The babies seemed normal at birth, but the peculiar shape of Margaret's eyes was noticed at that time.

Within a short time Margaret's trouble became apparent. At the age of 3 months "she just lay and took no notice." Some kind of shaking spasms developed; she did not sit up until she was a year old, did not walk until 3 years and did not talk until she was nearly 4. She was admitted to the State School at Wrentham, Mass., on July 24, 1925. There she was observed to present all the characteristics of mongolism. A Stanford-Binet test administered there on Oct. 21, 1929, revealed an intelligence quotient of 23. She was sickly from the beginning, with a special predisposition to respiratory troubles; pulmonary tuberculosis finally developed, and she died in the institution on Oct. 21, 1931.

Mildred presented a striking contrast in every respect. She developed normally both physically and mentally, graduated from high school and business college and has since earned her living as a secretary. The twins were different in features, stature and color of hair.

CASE 3.—*Opposite-sex twins, boy affected.*

The L. twins, Richard W. and Charlotte E., were born in Los Angeles on March 29, 1932. The father was 25 years old and the mother 26 at the time the twins were born. This was the mother's first pregnancy. There was no history of genito-urinary troubles in either parent. The mother's menstruation began at 11 years and had been regular and normal. Her pregnancy was uneventful, but was terminated one month "to the day" ahead of the expected time. The abdomen was greatly enlarged, but it was not known until one week before birth that she was carrying twins; then it was discovered by noting the two distinct heart beats and by roentgen examination. Richard was the first born (head presentation; normal delivery; no instrumentation); his weight at birth was 3 pounds and 10¾ ounces (1,666 Gm.). For twelve days both children were fed with a tube or by bottle, mother's milk being used, "on account of their being so tiny and weak." On the thirteenth day Charlotte began to nurse from the breast; there was considerable difficulty for about a week, but thereafter she nursed well and gained well. She also received additional feeding. At the time of our examination of the twins (Jan. 6, 1933) Charlotte weighed 16 pounds and 13 ounces (6,265 Gm.); the average normal weight for that age is 18 pounds (8,165 Gm.). Charlotte seemed to be developing normally; she stood by holding on to things, noticed things about her and recognized people. About ten days previously her first tooth had appeared, in the lower jaw.

Richard was not brought in for breast feeding until he was 3 weeks old. There was great and prolonged difficulty in getting him to nurse until he was 2 months old; "he wanted to sleep all the time." He gained well, however, and at the time of examination weighed 17 pounds and 8 ounces (7,938 Gm.). He had been heavier than Charlotte from the end of the third month. Mentally his development was not normal. The mother stated: "He is very slow to notice people; can't stand up, can't even sit alone; sleeps a great deal, and is just begin-

ning to make efforts to roll over or tumble a little, whereas his sister began doing that at least two months ago." He had no teeth. Mongoloid features had been noticeable from birth. He was "subject to chest colds." The mother said: "He seems to have a cold most of the time, coughs most of the time, has a hard time breathing and wheezes a great deal."

A Kuhlmann intelligence test was administered to the twins, with the following results: Charlotte, chronological age, 9.3 months, and mental age, 10.8 months—intelligence quotient, 119; Richard, chronological age, 9.3 months, and mental age, 4.8 months—intelligence quotient, 52.

A further communication from the mother received on July 22, 1933, states: "Charlotte has been walking since June 1. Richard can stand only by holding on to things, and he can crawl. He does such things as 'pat-a-cake' and 'so big,'

The L twins, Charlotte E. and Richard W. (case 3).

which Charlotte did months ago. He is in much better health as regards his breathing difficulty." A picture taken of the twins shortly after they were 11 months old is reproduced here.

CASE 4.—*Opposite-sex twins, boy affected.*

The F. twins, William Beattie and Beatrice, were born in Palmerston, Ontario, Canada, on Nov. 23, 1914. Birth was premature by five weeks. The children were bottle fed, and there was a great deal of nutrition difficulty with both. Beatrice was normal mentally and showed no evidence of mongolism; she died, however, at the age of 4 years of stomach trouble and malnutrition.

William B. presented obvious signs of mongolism from the beginning. On July 16, 1929, he was admitted to the Ontario Hospital at Orillia, where his case was immediately classified as one of mongolism. An intelligence test on July 31, 1929, revealed an intelligence quotient of 18. He was discharged from Orillia on Sept. 15, 1929, for transfer to a private institution.

CASE 5.—*Opposite-sex twins, boy affected.*

The D. twins, John Albert and Helen Louise, were born in San Diego, Calif., on March 12, 1930. Four children were born in this family before the twins, all normal. Both twins were delivered by breech presentation. Helen Louise developed normally and at the time of our observation (May 11, 1931) was bright and healthy.

John Albert was recognized as presenting mongolism a day or two after his birth. He was never removed from the hospital to his home because the parents feared the effect of the abnormal child on their 5 other children. He was transferred from the general hospital in which he was born to a private institution on July 20, 1930. From there he was transferred to the Pacific Colony at Spadra (the southern California state institution for the feebleminded) on Jan. 22, 1931. Almost immediately on his admission to the Pacific Colony bronchopneumonia developed, and he died on Jan. 27, 1931.

FOUR OTHER CASES

CASE 6.—*Male twins, type unascertained, one affected.*

The S. twins, William H. and Richard, came to our notice in July 1932. They have since been reported on by Hopwood.[1] We are republishing the report here in order that our readers may have ready access to it, as most medical libraries do not have in their files the bulletin in which it originally appeared.

The twins were born in Pennsylvania on April 16, 1919, at which time the mother was 39 and the father 52. This was the mother's fifth and last pregnancy. William H., the mongolian boy, was born first, and a few hours later his normal brother, Richard.

The original report stated: "The twins were of like sex and were probably of the double ovum type, but we were not able to establish this point with certainty. The normal twin weighed a pound less than his mongol brother, but developed into a healthy, robust child who talked, walked and had his teeth as a normal boy. He is described as a hustler who helps to milk and do the chores about the farm home. At the age of 13 years he is in the seventh grade. William, however, the mongol twin, although he was a plump, healthy looking child at birth, soon dwindled to a mere frame. He became listless, apathetic and was fed with difficulty. Respiratory troubles soon developed which were only partially relieved by the removal of his tonsils and adenoids. He did not walk until he was four years of age and has never learned to talk."

He was admitted to the Institution for the Feeble-minded at Orient, Ohio, on Nov. 26, 1929, and is still an inmate there. "He has made no progress; he is a low-grade, untidy idiot who cannot feed or dress himself." A Stanford-Binet test on April 7, 1932, revealed an intelligence quotient of 15.

CASE 7.—*Monozygotic female twins, both affected.*

This case was casually mentioned by Stransky[2] in a recent article dealing not especially with mongolism but with pathologic conditions in twins in general. We are introducing a special reference to this case here, as it might readily be overlooked in a survey of the literature pertaining to mongolism in twins.

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1. Hopwood, Arthur T.: Etiology of Mongolism, Quart. Bull. Managing Off. Assn. Dept. Pub. Welfare, State of Ohio, December 1932.

2. Stransky, Eugen: Beiträge zur Zwillingspathologie: Part II, Monatschr. f. Kinderh. **48**:183, 1930.

CASE 8.—*Monozygotic female twins, both affected.*

This case was first reported by Bodil Hjorth about twenty-five years ago, but no information was then submitted with reference to the type of the twins.[3] In 1926 Krabbe[4] published a further report on these twins in which he furnished information to the effect that they were in all probability monozygotic. They could hardly be told apart by those who were in daily contact with them; a picture of them printed in Krabbe's article shows them to be practically identical in appearance. They died of tuberculosis, one in November 1922 and the other in February 1923. We are introducing a special reference to this case here in order to transfer it from the classification "type unascertained" to that of monozygotic type.

CASE 9.—*Monozygotic male twins, both affected.*

This case was reported by Reuben and Klein[5] in 1926. Here, too, however, information as to type was not furnished. We have been able to secure data from the records of the Jewish Maternity Hospital in New York, where these twins were born, indicating that they may be transferred from the classification "type unascertained" to that of monozygotic type. They were born at full term, about fifteen minutes apart. The birth weights were 6 pounds and 4 ounces (2,841 Gm.) and 4 pounds and 3 ounces (1,899 Gm.), respectively. There was only one placenta, delivered five minutes after the birth of the second twin.

SUMMARY OF ALL PUBLISHED CASES

In her monograph on mongolism, published in 1928, Brousseau[6] submitted a table in which were summarized 37 cases of mongolism in twins reported in the literature up to that time. Since then 22 additional cases have been reported, which, together with the 5 cases collected by us, make a total of 64 cases.

The cases[7] which have been reported since the appearance of the monograph by Brousseau are listed in table 1.

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3. Hjorth, Bodil, quoted by Shuttleworth, G. E.: Mongolian Imbecility, Brit. M. J. **2**:661, 1909.

4. Krabbe, Knud H.: La pathogénèse de l'idiotie mongoloïde en lumière de mongolisme chez les jumeaux, Acta psychiat. et neurol. **1**:337, 1926.

5. Reuben, Mark S., and Klein, Sidney: Mongolian Idiocy in Both Twins, Arch. Pediat. **43**:552, 1926.

6. Brousseau, Kate: Mongolism, Baltimore, Williams & Wilkins Company, 1928.

7. Dickey, L. B.: Mongolism in Both Twins, California & West. Med. **26**:344 (March) 1927. Chown, G.: Mongolian Idiocy in One of Male Twins, Canad. M. A. J. **17**:943 (Aug.) 1927. Armstrong, Hubert: Etiology of Mongolism, with a Case of Mongol Twin, Brit. M. J. **1**:1106 (June 30) 1928. Shattuck, R. H.: Mongolism in One Twin, J. A. M. A. **92**:1593 (May 11) 1929. Bauer, Alfred: Ueber die Aetiologie des Mongolismus anhand der bisherigen Ergebnisse der Zwillingserforschung, Arch. f. Kinderh. **90**:169 (May) 1930. Petzoldt, Gertrud: Mongolismus bei einem von Zwillingen, Monatschr. f. Kinderh. **47**:174, 1930. Waring, J. I.: Mongolism in One of Twins, Am. J. Dis. Child. **41**:351 (Feb.) 1931. Orel, Herbert: Mongolismus bei Zwillingskindern, Ztschr. f. Kinderh. **51**: 31, 1931. Adalid, E., and Escardó, F.: Mongolismo en un solo gemelar, Semana

(*Footnote 7 continued on following page*)

All the published cases of mongolism in twins are summarized in table 2. Among the early cases there are some in which the type and even the sex were unascertained.

TABLE 1.—*New Cases of Mongolism in Twins*

No.	Authors	Year	Sex of Twins	Type of Twins	Twins Affected
1	Krabbe	1926	Males	Dizygotic	One
2	Krabbe	1926	Females	Dizygotic	One
3	Krabbe	1926	Opposite-sex	Dizygotic	Boy
4	Krabbe	1926	Opposite-sex	Dizygotic	Girl
5	Dickey	1927	Males	Monozygotic	Both
6	Chown	1927	Males	Dizygotic	One
7	Armstrong	1928	Opposite-sex	Dizygotic	Boy
8	Shattuck	1929	Opposite-sex	Dizygotic	Girl
9	Bauer	1930	Females	Monozygotic	Both
10	Bauer	1930	Opposite-sex	Dizygotic	Boy
11	Petzoldt	1930	Females	Dizygotic	One
12	Stransky	1930	Females	Monozygotic	Both
13	Waring	1931	Opposite-sex	Dizygotic	Girl
14	Orel	1931	Females	Dizygotic	One
15	Orel	1931	Males	Dizygotic	One
16	Adalid and Escardó	1932	Males	Dizygotic	One
17	Blechmann, Gillaumin and Karmann	1932	Males	Monozygotic	Both
18	Hopwood	1932	Males	Unascertained	One
19	Legras	1932	Opposite-sex	Dizygotic	Girl
20	Legras	1932	Males	Dizygotic	One
21	Russell	1933	Females	Unascertained*	Both
22	Lund	1933	Females	Monozygotic	Both
23	Rosanoff and Handy	1934	Females	Monozygotic	Both
24	Rosanoff and Handy	1934	Females	Dizygotic	One
25	Rosanoff and Handy	1934	Opposite-sex	Dizygotic	Boy
26	Rosanoff and Handy	1934	Opposite-sex	Dizygotic	Boy
27	Rosanoff and Handy	1934	Opposite-sex	Dizygotic	Boy

* Reported by the author as dizygotic twins, but on insufficient evidence. See editorial in the Journal of Heredity (**24**: 281 [July] 1933).

TABLE 2.—*Summary of All Published Cases*

Type of Twins	Number of Cases	One Affected	Both Affected
Monozygotic, males	3	..	3
Monozygotic, females	5	..	5
Type unascertained, males	9	7	2
Type unascertained, females	6	4	2
Same-sex, dizygotic, males	6	6	..
Same-sex, dizygotic, females	7	7	..
Opposite-sex, dizygotic	23	23	..
Type and sex unascertained	5	5	..
Totals	64	52	12

méd. **39**:1823 (June 16) 1932. Blechmann, G.; Gillaumin, C. O., and Karmann, L.: Présentation de deux jumeaux mongoliens, Bull. Soc. de pédiat. de Paris **30**:387 (June) 1932. Orel, Herbert: Zur Aetiologie des Mongolismus, Ztschr. f. Kinderh. **42**:440, 1926. Legras, A. M.: Psychose en Criminaliteit by Tweelingen, Utrecht, Kemink en zoon, 1932. Russell, P. M. G.: Mongolism in Twins, Lancet **1**:802, 1933. Lund, S. E. Torsten: Mongolism in Monozygotic Twins, Am. J. Dis. Child. **46**:810 (Oct.) 1933.

SIGNIFICANCE OF THE TWIN MATERIAL

The earlier reports of cases of mongolism in twins were rendered apparently without a realization of their bearing on the question of etiology, but merely as curiosities met with in medical practice. To Halbertsma probably belongs the credit of being the first one to point out the value of such material for the elucidation of the origin of mongolism. In 1923 he had come to the conclusion that the theory of "uterine exhaustion" was untenable and that mongolism was germinal in origin.

Since then this view has gained ground with the accumulation of further material. It has been more or less clearly expressed by Orel,[8] Krabbe,[4] Armstrong,[9] Bauer,[10] Petzoldt [11] and others.

It seems, indeed, that the figures given in table 2 indicate clearly that mongolism must be produced by etiologic factors at work some time prior to that moment in the early part of the embryonic period of development at which, in cases of monozygotic twins, the division into two takes place.

The family histories in cases of mongolism definitely exclude hereditary, i. e., pregerminal [12] factors in its etiology. On this point practically all students of the subject are now in agreement. This narrows the possibilities down to factors which must be at work in the germinal or early embryonic period of development. The present status of the matter has been, perhaps, best stated by Orel:

> Since, on the one hand, the inheritance of mongolism is improbable and, on the other hand, its intrauterine origin can be excluded, one is forced to assume that some hitherto unknown sort of injuries to the germ cells or to the fertilized egg effect a quite definite tendency toward mongolism. Probably of significance, in this connection, is also the advanced age of the parents of mongoloid children, to which attention is bound to be drawn by all larger statistics.

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8. Orel, Herbert: Zur Aetiologie des Mongolismus, Ztschr. f. Kinderh. **42:** 440, 1926.

9. Armstrong, Hubert: Etiology of Mongolism, with a Case of Mongol Twin, Brit. M. J. **1:**1106 (June 30) 1928.

10. Bauer, Alfred: Ueber die Aetiologie des Mongolismus anhand der bisherigen Ergebnisse der Zwillingserforschung, Arch. f. Kinderh. **90:**169 (May) 1930.

11. Petzoldt, Gertrud: Mongolismus bei einem von Zwillingen, Monatschr. f. Kinderh. **47:**174, 1930.

12. The distinction between pregerminal and germinal factors in etiology has not been sufficiently emphasized. The factors which we designate as pregerminal are the only ones which may properly be spoken of as hereditary. They are the factors which have determined their effects in the bodies of the immediate and remote ancestors of a given generation before that generation enters on the beginning of its existence in the form of primordial follicles in the ovary or of spermatocytes in the testis.

AGE OF PARENTS

In all discussions of the etiology of mongolism the parents' age is shown to be a factor. Thus in the series of cases reported by Brousseau [6] the ages of 457 fathers at the time of birth of their mongolian children were ascertained and were divided as follows:

Under 30 years	67	(14.7%)
30 years or over	390	(85.3%)

Similarly, the ages of 584 mothers were divided as follows:

Under 30 years	137	(23.5%)
30 years or over	447	(76.5%)

The corresponding figures for the unselected population, according to the United States census,[13] are as follows:

Fathers under 30 years	967,904	(46.5%)
Fathers 30 years or over	1,111,472	(53.5%)
Mothers under 30 years	1,431,383	(67.5%)
Mothers 30 years or over	687,680	(32.5%)

A more detailed examination of data pertaining to this matter reveals that the factor of importance is the age of the mother and not that of the father. The age of the father apparently has no direct bearing on the etiology of mongolism, but only an indirect one by reason of its being, naturally, in close correlation with the mother's age. This may be judged from the statistics given in table 3, taken from an English public health report for 1925.[14]

It would be difficult by a mere inspection of the array of figures in the table to disentangle the respective effects of the fathers' and mothers' ages. The procedure that suggests itself as an aid in this connection is to classify the parents of the mongolian children into four groups according to their relative ages and to compare them with similarly classified parents in the unselected population. The results of such a procedure are given in table 4. The figures for the unselected population have been derived from the United States census.[13]

It will be seen from table 4 that the group in which both parents are young is relatively nearly six times as large in the unselected population as it is in the parents of mongolian children. On the other hand,

13. Birth, Stillbirth and Infant Mortality Statistics for the Birth Registration Area of the United States, 1929, 15th Ann. Rep., U. S. Dept. Commerce, Bur. Census, 1932, p. 11.

14. London County Council Public Health Reports, 1925, quoted by Hogben, L.: Genetic Principles in Medicine and Social Science, New York, Alfred A. Knopf, 1932.

the group in which both parents are of advanced age is relatively nearly three times as large in the parents of mongolian children as it is in the unselected population.

It will be seen, further, that the group in which the fathers alone are of advanced age is more than four times as large, relatively, in the unselected population as it is in the parents of mongolian children, whereas the group in which the mothers alone are of advanced age is relatively larger in the parents of mongolian children than in the unselected population, although here the number of cases is so small that one could not be sure of the validity of the statistics.

TABLE 3.—*Ages of Parents of 294 Children with Mongolism*

Mother's Age	Father's Age												
	18-20	21-23	24-26	27-29	30-32	33-35	36-38	39-41	42-44	45-47	48-50	Over 50	Total
18-20	..	1	1	..	..	..	..	..	..	..	..	..	2
21-23	..	3	2	..	1	..	..	..	..	..	..	..	6
24-26	..	..	2	..	4	2	..	..	..	..	..	..	8
27-29	..	..	1	13	4	1	2	1	..	..	..	..	22
30-32	..	..	..	2	9	7	2	2	..	..	..	..	22
33-35	..	..	..	1	2	11	8	4	1	1	1	1	30
36-38	..	..	..	2	2	8	18	14	6	3	2	3	58
39-41	..	..	..	..	1	4	7	31	15	5	2	2	67
42-44	..	..	..	..	..	3	1	9	20	14	9	5	61
45-47	..	..	..	..	..	..	1	..	3	4	6	3	17
48-50	..	..	..	..	..	..	..	..	..	..	1	..	1
Over 50	..	..	..	..	..	..	..	..	..	..	..	..	..
Total	..	4	6	18	23	36	39	61	45	27	21	14	294

TABLE 4.—*Unselected Parents and Parents of Mongolian Children Classified by Relative Ages*

Groups	Unselected Parents		Mongolian Children's Parents	
	Number	Per Cent	Number	Per Cent
Both parents under 30	963,010	44.2	23	7.8
Both parents 30 or over	727,231	33.4	251	85.4
Father 30 or over, mother under 30	456,688	21.0	15	5.1
Father under 30, mother 30 or over	30,041	1.3	5	1.7
Total	2,176,970	100.0	294	100.0

The special importance of the mother's age, and not the father's, in the etiology of mongolism suggests that the hypothetic injury causing this condition is not to the spermatocyte or the spermatozoon but to the ovum. Armstrong [9] went even further and was more specific in his opinion: "I believe the maternal influence, which appears to be almost undeniable, and whatever it may be, is exercised upon the ovum during its maturation and therefore before fertilization has followed and segmentation started."

ORDER OF BIRTH

In general, the incidence of mental deficiency and of certain other neuropathic conditions is higher among the first-born than among the later-born children. In regard to mongolism the reverse is the case, and some theories of etiology have been based on that fact.

The correlation between the incidence of mongolism and the order of birth is clearly shown by the figures given in table 5, also taken from the English public health report for 1925,[14] previously cited. It will be seen that up to the fourth place in order of birth the number of cases of mongolism that have occurred is markedly below the calculated expec-

TABLE 5.—*Order of Birth of 314 Children with Mongolism*

Place in Family	Number of Children in Family																Mongolism Cases	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Actual	Expected*
1	13	12	7	5	2	..	..	1	..	..	..	..	..	..	..	..	40	72
2	..	22	13	1	1	..	..	..	..	..	..	..	..	..	..	..	37	60
3	..	..	19	8	3	..	2	2	..	..	..	..	..	..	..	..	34	45
4	..	..	..	25	7	2	..	..	..	..	..	..	..	..	..	..	34	33
5	..	..	..	..	28	6	4	2	..	..	..	..	..	..	..	..	40	24
6	..	..	..	..	..	20	4	2	1	..	..	..	..	..	..	..	27	17
7	..	..	..	..	..	..	20	2	5	..	..	..	..	..	..	..	27	13
8	..	..	..	..	..	..	..	15	2	2	1	..	..	..	..	..	20	8
9	..	..	..	..	..	..	..	..	13	1	1	..	1	1	..	..	17	6
10	..	..	..	..	..	..	..	..	..	7	3	1	1	..	..	..	12	4
11	..	..	..	..	..	..	..	..	..	..	7	2	2	2	..	..	13	3
12	..	..	..	..	..	..	..	..	..	..	..	3	..	..	..	..	3	2
13	..	..	..	..	..	..	..	..	..	..	..	..	3	3	..	..	6	1
14	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	..	2	1
15	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	0.2
16	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	2	0.1

* "If it is equally likely that a first, second, third, etc., child will be a mongol, the expected number of first children will be $n_1 + \frac{1}{2}n_2 + \frac{1}{3}n_3 + \frac{1}{4}n_4$. . . . The expected number of second children will be $\frac{1}{2}n_2 + \frac{1}{3}n_3 + \frac{1}{4}n_4$. . . . The expected number of third children will be $\frac{1}{3}n_3 + \frac{1}{4}n_4 + \frac{1}{5}n_5$. . . . and so on, n_1, n_2, n_3 . . . being the number of fraternities with one, two, three, . . . sibs." [14]

tancy whereas from the fourth place on the number exceeds the expectancy in increasing measure.

We are here again confronted with a situation in which the effects of two closely related factors—age of the mother and order of birth—must be disentangled before we can arrive at a judgment as to their relative importance in etiology.

In this connection, it should be noted first of all that, if late order of birth is a factor in the etiology of mongolism, it is not an essential factor. Nearly one fourth of Brousseau's series of 800 cases occurred in first-born children, as did also 40 of the 314 English cases cited in table 5.

It should be noted further that, while a mongolian idiot is often the last born of a family of children, this is by no means invariably the case. As may be seen from table 5, in 185 families of 2 or more children the

mongolian child was the last born, but in 106 families the birth of the mongolian child was followed by the birth of from 1 to 7 nonmongolian children.

What importance, then, has the factor of order of birth? In order to be in a position to answer this question it is necessary first to eliminate the factor of the mother's age.

It is not easy to find the statistical data required for our purpose. The largest single collection of material was gathered by Brousseau. She gave in one table [15a] the order of birth in 800 cases of mongolism. This makes possible an enumeration of the number of families represented and their classification according to the size of family at the time of the birth of each mongolian child.

Unfortunately the ages of the mothers are not given in this connection. In another table [15b] are given the ages of 584 mothers of mongolian children.

Assuming that the ages of the mothers of the entire group of 800 mongolian children are distributed approximately like those of the 584 whose ages are known, it appears that the ages of the mothers in the 800 cases were probably as follows:

Age in Years	No. of Mothers
15-19	26
20-24	79
25-29	82
30-34	119
35-39	187
40-44	238
45-49	63
50 or over	6

According to the United States birth statistics,[16] the average numbers of children per mother, respectively, for these age groups in the unselected population are as follows: 1.3, 2, 3, 4.2, 5.8, 7.4, 8.9 and 8.1. These figures are for mothers of children born in 1929, not including stillbirths of that year. The averages represent all of the chidren born and not merely the children living in that year. In other words, these statistics are, like those pertaining to the 800 children with mongolism, based strictly on order of birth.

We find by computation that 800 mothers in the unselected population of the same age distribution as the mothers of mongolian children in Brousseau's collection would have borne a total of 4,393 children.

However, the 800 mothers of mongolian children had actually borne only 3,252 children, indicating that, on the whole, mothers of mongolian

15. Brousseau, Kate: (*a*) Mongolism, Baltimore, Williams & Wilkins Company, 1928, p. 31; (*b*) ibid., p. 28.

16. Footnote 13, p. 248.

children actually have fewer children than mothers of the same ages in the unselected population.

Thus the result of the analysis is to the effect that the size of the family, the order of birth, "uterine exhaustion," etc., play no part in the etiology of mongolism; they stand out in the statistics only by reason of their correlation with the one real factor—the age of the mother.

SEX

If it is true that mongolism is produced by a germinal factor causing injury to the ovum and not to the spermatozoon, it appears, nevertheless, that the spermatozoon is not without its influence. This is suggested by the unequal sex distribution of mongolism.

That mongolism is definitely more common in boys than in girls has been reported by all students of the subject. For example, Orel,[8] in surveying the literature, brought together figures furnished by a number of observers, including his own, showing that of a total of 1,198 cases 715 were in boys and 483 in girls.

This relative excess of mongolism in boys, amounting apparently to 48 per cent, has never been explained. Many writers are of the opinion that it is apparent rather than real, because the reported cases represent, for the most part, institutional material, and, it is said, males are, for sociologic reasons, more likely than females, to enter institutions.

This view does not dispose of the matter, not only because of the practically constant fact of uneven distribution observed both among institutional cases and among cases seen in outpatient clinics and in private practice, but because the contrast is even more marked between opposite-sex twins. Among the 23 cases of mongolism in opposite-sex twins reported in the literature (including our 3 cases reported in this communication) the girl was affected in 9 cases and the boy in 14 cases—a relative excess of 55 per cent in the boys.

It seems from this that in some cases an ovum which on fertilization by a male-producing spermatozoon (one with a Y-chromosome) would result in a mongolian child is protected against such a development on fertilization by a female-producing spermatozoon (one with an X-chromosome).

Why, then, is not mongolism strictly sex limited, or, in other words, why are not all girls protected against it? It may be that protective genes in X-chromosomes are carried only in certain familial strains and not in others; it may be that the amount of damage to the ovum is slighter in some cases than in others and therefore more readily repaired; or it may be that both factors come into play to a greater or lesser relative extent.

We have already pointed out, in previous communications,[17] that there is evidence suggesting the existence, in some cases, of sex-linked factors of intelligence. It may be that such factors are concerned also in the protection of some girls against mongolism.

However this may be, two readily demonstrable facts concerning mongolism should receive consideration in this connection: first, that the germinal damage which manifests itself in mongolism varies in degree, and second, that mongolism in girls is, as a rule, milder than that in boys.

The degree of severity of cases of mongolism may be roughly measured with the aid of two criteria: age at death and results of intelligence tests.

TABLE 6.—*Distribution of Intelligence Quotients for Males and Females with Mongolism*

Intelligence Quotients	Males		Females	
	Number	Per Cent	Number	Per Cent
Under 20	36	27.3	19	25.7
20 to 39.5	85	64.4	45	60.8
40 or over	11	8.3	10	13.5
Total	132	100.0	74	100.0

As regards age at death, it is well known that more than half of the persons with mongolism die during childhood. The rest also die early, and it is rare to find a mongolian idiot over 30 years of age in an institution. Among 165 cases reported by Brousseau the ages at death were distributed as follows:

Age in Years	No. of Cases
Under 5	66
5-9	24
10-14	24
15-19	14
20-24	16
25-29	9
30 or over	12

As regards the results of intelligence tests, the intelligence quotients of 206 persons with mongolism, reported by Brousseau, varied between the extremes of 7 and 66 and were distributed for the two sexes as shown in table 6.

17. Rosanoff, A. J.: Sex-Linked Inheritance in Mental Deficiency, Am. J. Psychiat. **11**:289 (Sept.) 1931. Rosanoff, A. J.; Handy, L. M.; Rosanoff, I. A., and Inman-Kane, C. V.: Sex Factors in Intelligence, J. Nerv. & Ment. Dis. **80**:125 (Aug.) 1934.

PATHOGENESIS OF MONGOLISM

All the known facts concerning mongolism seem to point to some condition in the ovary as underlying its pathogenesis. Perhaps a systematic pathologic investigation of the ovaries of women who have given birth to mongolian idiots—whenever an opportunity for doing so might present itself—would throw some light on the matter. As yet no such investigation has been made, to our knowledge.

We have, however, a sufficient amount of circumstantial evidence, to borrow a legal term, to justify the speculation that *foci of tissue change —perhaps scars—marking the sites of old ovulation are the cause of the trouble.*

Accordingly, the ovaries of any girl who has menstruated one or more times contain one or more foci at which injury to an ovum may occur such as to lead to mongolism.

TABLE 7.—*Sizes of Families With and Without Mongolism*

Number of Children in Family	Percentage for Mongolian Children Born	Percentage for Nonmongolian Children Born
1 to 3	56.5	74.6
4 to 6	20.3	18.3
7 to 9	17.0	5.2
10 to 12	5.0	1.5
13 to 15	1.1	0.4
Over 15	0.1	0.1

By this theory, the chance of producing a child with mongolism increases with the passing of each menstrual period—which, of course, harmonizes with the correlation of the incidence with the age of the mother.

As mongolism is rare even among children of mothers of late middle age, it must be judged that the chance of corresponding injury to an ovum is still slight in the presence of one hundred and fifty or more old ovulation foci. The extreme rarity of the occurrence of more than 1 case of mongolism in a family shows that the chance of producing such a defective ovum is remote even in the case of an ovary which is demonstrably capable of doing so.

A consequence of the theory here proposed is that the chance of a given mother's having a mongolian child increases with her number of children. This is true not only because with the increase of the family the mother's age also increases but because of simple multiplication of hazards. In other words, ignoring, for the moment, the factor of the mother's age, if the hazard of producing a mongolian child under certain conditions amounts to, say, one chance in a thousand, the hazard is doubled if two children are born, trebled in case of three children, etc. This is clearly shown by comparing the sizes of families in which there

are mongolian idiots with those of the unselected population. In table 7 we submit the figures for such a comparison. The percentages for families in which there are mongolian idiots have been derived by calculation from data pertaining to the order of birth of 800 persons with mongolism as given by Brousseau.[6] The corresponding percentages for the unselected population have been derived by similar calculation from data pertaining to the order of birth of children born in 1929 given in the birth statistics of the United States census for the State of California.[18] It will be seen that families of from 1 to 3 children are relatively less frequent among those of mongolian idiots than in the unselected population, whereas larger families are increasingly more so.

It seems impossible to incriminate coarse lesions of the ovary, such as large cysts or tumors or diffuse processes of sclerosis or atrophy, whether occurring as presenile changes or as residuals of infection. In order to harmonize with known facts, our theory must, on the contrary, assume that in a mother of any age who has given birth to a mongolian idiot the bulk of the ovarian tissue is normal, and that only small discrete foci, constantly forming and accumulating throughout the childbearing period, bring with them, in normal women, a hazard of producing a mongolian child—a hazard which at first is almost infinitesimal but which grows steadily, although ever remaining small.

SUMMARY

Five new cases of mongolism in twins are reported.

A summary is presented of all cases of mongolism in twins reports of which have been published—64, including our 5 cases.

The etiologic factors of mongolism are narrowed down to those that must be at work in the germinal or early embryonic period of environment.

There is definite statistical correlation between the incidence of mongolism and the age of the parents. An attempt is made here to show, however, that the real etiologic factor is the age of the mother, that of the father having only an indirect bearing by reason of being in statistical correlation with the age of the mother.

Similarly, the size of the family, the order of birth, "uterine exhaustion," etc., play no part in the etiology of mongolism; they stand out in the statistics only by reason of their correlation with the one real factor—the age of the mother.

Mongolism is more common among boys than among girls. This finding is so constant as to force us to assume that, although injury to the ovum is the essential cause of mongolism, the spermatozoon is not without its influence. The X-chromosome in the female-producing

18. Footnote 13, p. 227.

spermatozoon seems to have, in some cases, the power of protecting an injured ovum against its tendency to develop into a mongolian child. In this connection it is pointed out that monogolism varies greatly in the severity of its manifestations and is, on the whole, milder in girls than in boys, possibly owing to partial protection by the additional X-chromosome.

All the known facts concerning mongolism seem to point to some condition of the ovary as underlying its pathogenesis. No systematic pathologic investigation of the ovaries of women who have given birth to mongolian idiots has been made, to our knowledge. Coarse or diffuse lesions seem to be excluded as a possible cause. All available evidence seems to justify the speculation that *foci of tissue change—perhaps scars —marking the sites of old ovulation are the cause of the trouble.*

THORACIC AORTIC ANEURYSMS IN CHILDREN

THEIR RELATION TO RHEUMATIC FEVER

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Aneurysms of the thoracic aorta in children, though rare, occur frequently enough to warrant attention, because a group of them are a part of the much more common rheumatic fever syndrome. A great diversity of opinion has existed regarding the etiology of the thoracic aneurysm in the young. Some authors have believed that syphilis is practically always the prime factor in children as in adults, but a careful study of the available cases does not confirm this view.

The etiologic factors in the production of aortic aneurysms in childhood have been classified by Bronson and Sutherland [1] in the following manner: (1) atheromatous degeneration; (2) trauma (rare); (3) erosion of the aorta from without; (4) congenital malformation (in a few cases), and (5), probably the most important, acute infectious diseases.

Up to the present forty-four cases of aneurysm of the thoracic aorta in persons under 18 have been reported. In twenty-one of the cases there was an association with endocarditis (ten instances) or clinical rheumatic fever (eleven). In all of the cases of the former group autopsies confirmed the presence of lesions in the endocardium as well as in the aorta. In the latter group autopsy was performed in only one case, in which in addition to a dissecting aneurysm of the aorta there were mild coarctation and acute pericarditis with hemopericardium; a year before death the patient had pains and swelling of the joints.[2] Two cases of this group were seen and reported by one of us (J. K. C.[3]); the patients gave a definite history of rheumatic fever and there were physical findings of rheumatic heart disease. Evidence

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From the Department of Pediatrics of the University of Illinois Medical School and the Children's Department of Cook County Hospital.

1. Bronson, E., and Sutherland, G. A.: Ruptured Aortic Aneurysms in Childhood, with Report of a Case, Brit. J. Child. Dis. **15**:16 (Oct.-Dec.) 1918.

2. Narr, F. C.: Acute Infective Aortitis, Am. J. Dis. Child. **45**:447 (Feb.) 1933.

3. Calvin, J. K.: Aneurysms of the Thoracic Aorta in Children, Am. J. Dis. Child. **21**:327 (April) 1921.

of syphilis was present in two cases, in one [4] of which there was confirmation by autopsy. In the other case (Heiman's [5]) there was a definite history of several attacks of acute articular rheumatism as well as a positive Wassermann reaction and clinical evidence of syphilis. Trauma was noted as the cause in two cases,[6] but this diagnosis was not confirmed by autopsy. Erosion of the aorta from without by caseous and suppurating lymph glands occurred in five cases.[7] In five others the condition was associated with congenital malformation of the aorta in the form of stenosis near the ductus arteriosus, the degree of stenosis varying from coarctation to moderate uniform narrowing.[8] Mechanical factors probably participate in the production of an aneurysm proximal to congenital stenosis of the thoracic aorta, especially if that portion of the aortic wall has been weakened by an infectious process.

The predominance of rheumatic fever as an etiologic factor in the production of thoracic aortic aneurysms in the young is thus apparent from a review of the literature, almost half of all the reported cases being in the rheumatic fever group. The susceptibility of children to infections associated with rheumatic fever is well known. A result of the pathologic changes is demonstrable at times in the form of verrucae on the intimal lining of the thoracic aorta, as in our cases, or as a primary involvement of the adventitia and media along the vasa vasorum with cellular infiltration and necrosis. The end-result of such changes in the aorta may be the formation of a typical saccular aneurysm or a weakening of the aortic wall with dilatation, with or without rupture. The rheumatic syndrome in childhood should therefore include a consideration of the symptoms and signs produced by such lesions of the thoracic aorta.

The two cases reported demonstrate lesions of this type.

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4. Willson, R., and Marcy, A.: Proc. Path. Soc., Philadelphia **16**:63, 1914.

5. Heiman, H.: Aneurysm of Ascending Arch of Aorta in a Boy of Thirteen, Arch. Pediat. **36**:543 (Oct.) 1919.

6. MacKeen, R. A. L.: M. News **61**:272, 1892. Pendin, A.: Ein Fall von Aneurysm Aortae Ascendenti bei einem 12 jährigen Mädchen, St. Petersburg med. Wchnschr. **7**:195, 1890.

7. (*a*) Hutchinson: Tr. Path. Soc., London **5**:104, 1854. (*b*) Smith, F. J.: Aneurysm of Aorta in a Boy of Nine Years, ibid. **48**:53, 1897. (*c*) Willett, E.: Aneurysm of Aorta in Child of Four Years, ibid. **43**:38, 1892. (*d*) Clarke, Jackson, quoted by Calvin.[3]

8. Wassajerna, E.: Ein Fall von Aortaruptur nach Schlittschuhlaufen, Ztschr. f. klin. Med. **90**:405, 1903. Horder, T. J.: Dissecting Aneurysm of the Aorta in a Boy, Aged 12: Rupture into Pericardium, St. Barth. Hosp. Rep. **43**:57, 1908. Richey, deW. G.: Intrapericardial Rupture of Aortic Aneurysm in a Boy, 16 Years of Age, Arch. Int. Med. **31**:232 (Feb.) 1923. Bronson and Sutherland.[1] Smith.[7b]

REPORT OF CASES

CASE 1.—An Italian girl, aged 11 years, entered the Cook County Hospital on March 8, 1932. She was apparently well until one week prior to entrance, when pain over the heart, cough and fever developed. On the day of entrance into the hospital she had a moderate nosebleed.

The birth and developmental history were inconsequential. The child had measles and chickenpox. There were no miscarriages in the family history. The parents said that they had never had a venereal infection.

On physical examination, the patient appeared well nourished but somewhat underdeveloped. The temperature was 102.4 F., the pulse rate 124, the respiratory rate 28 and the blood pressure 140 systolic and 60 diastolic. Herpes was present over the left ala nasae. The tonsils were enlarged. Coarse râles could be heard over the left base. Breath sounds in the right side of the chest were diminished. The heart was enlarged transversely, and there were a soft, systolic thrill and a systolic and diastolic murmur over the apex. The pulse at the wrist was forceful, of high pressure, quickly striking the finger and receding. The carotid pulsations were easily visible. The pulsations in the popliteal, dorsalis pedis and posterior tibial arteries were not palpable, nor could they be detected by the blood pressure apparatus. There were no visible or palpable arteries in the flanks or axillae. The liver was palpable 1 fingerbreadth below the right costal border. The spleen was not palpable. The white blood cell count was 20,100, with 84 per cent polymorphonuclear leukocytes, 14 per cent lymphocytes and 2 per cent monocytes. There were many macrocytes present. Polychromatophilia and anisocytosis were evident. The urine was normal, and the Kahn test of the blood was negative. The Pirquet test was negative. Urea nitrogen was 16.34 mg. per hundred cubic centimeters. Blood culture showed no growth. The roentgenographic report stated that the heart showed marked enlargement, and that there was passive congestion in the pulmonary fields.

The clinical diagnosis was endocarditis of the aortic and mitral valves, bronchopneumonia and coarctation of the aorta.

Two days later the temperature dropped to normal and then fluctuated between 99 and 100 F., the respiratory rate from 40 to 60 and the pulse rate from 120 to 140. Impaired thoracic resonance, râles and bronchovesicular breathing persisted and became more diffuse. Coughing was frequent, severe and nonproductive. One week after admission the child was seen sitting up in bed and resting quietly but coughing frequently. Forty-five minutes later she was found on the floor dead.

Autopsy (Dr. R. H. Jaffé and Dr. B. H. Neiman).—The essential observations were in the heart and aorta.

The heart weighed 250 Gm. The wall of the left ventricle measured 12 mm., and that of the right ventricle 5 mm., in thickness. The epicardium was thin, transparent, smooth and shiny. The apex was formed by the left ventricle. The myocardium was purple-gray and friable. The transverse and vertical diameters of the left ventricle were 8.5 cm. The trabeculae and papillary muscles were slightly flattened. On the auricular surface of both cusps of the mitral valve were pinhead-sized, granular, firm and slightly transparent nodules. The free edges of the aortic leaflets were thickened and rounded, and along the limbus there were firm, sandlike granular deposits.

The aorta measured 52 mm. in circumference above the valve. About 1 cm. above the aortic valve there was an oblique, transverse tear which was 35 mm. in width. The edges of the tear were indented, and a 2 mm. longitudinal bridge of

intact wall separated the tear into a larger right portion and a smaller left portion. The floor of the tear exposed a thin, pink-gray membrane with fine, longitudinal lines and small, granular elevations. The adventitia was injected. To the right, the tear terminated in an irregular, slightly depressed, light brown area. In the ascending aorta there were several streaklike, light-yellow areas as large as 25 by 4 mm. Just beyond the origin of the left subclavian artery, the lumen of the aorta suddenly became narrowed to a diameter of about 1 mm. Beyond the narrowed portion, the circumference of the aorta widened to about 58 mm. Small, light-yellow plaques were found in the upper wall of the arch. At the diaphragm, the circumference of the aorta was 36 mm.; below the origin of the renal arteries it was 22 mm.

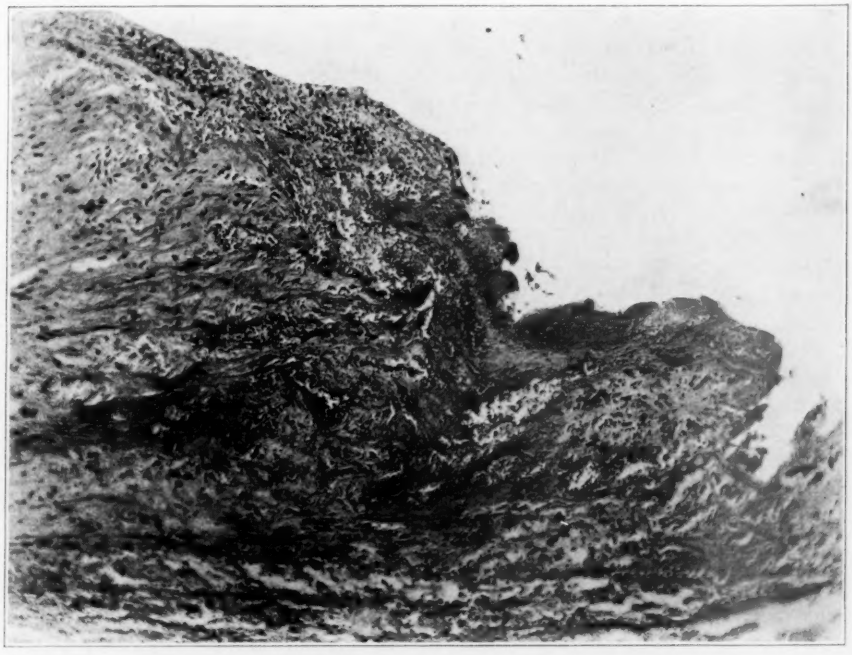

Fig. 1 (case 1).—Section taken from the aorta at the point of rupture (× 150). The intima is thickened, owing to cellular accumulations between the endothelium and the internal elastic membrane. The internal elastic membrane is split into several layers and in one place is completely interrupted. Near the torn portion, the muscle fibers and elastic fibers of the media pass rather abruptly into a zone of complete necrosis without structural differentiation.

Microscopic Examination.—The tear in the ascendens portion of the aorta involved the intima and the entire media and exposed the adventitia which was densely infiltrated by polymorphonuclear leukocytes. Approaching the tear, the intima became slightly thickened, and in the region of the tear was everted, covering the edges of the torn structures. The thickening of the intima resulted from a cellular accumulation between the endothelium and the internal elastic membrane. Delicate elastic fibrils were separated by swollen fibrocytes with large pale nuclei, small round cells and histiocytic elements with an ample cytoplasm and round or oval nuclei. Bizarre-shaped, drawn-out nuclei were lying free between the intact

cells. The internal elastic membrane was split into several layers and in the everted portion showed areas of fraying until it was completely interrupted. Near the torn portion, the muscle fibers and elastic fibers of the media passed rather abruptly into a zone of complete necrosis without structural differentiation and scanty chromatin granules. In the outer portion of the media, single mononuclear elements were wedged in between trabeculae of necrotic tissue, and the necrosis extended for a short distance beyond the tear along the external elastic membrane. In the floor of the defect there were only a few small segments of the external elastic membrane visible.

Between the polymorphonuclear leukocytes which infiltrated the adventitia, one found single, large, degenerating fibrocytes, the nuclei of which assumed irregular forms. Elastic fibrils were practically absent.

Away from the tear, the intima appeared well preserved. In the media there were circumscribed areas of increase of the metachromatic substance which spread apart the elastic elements. Near the outer elastic membrane there were small areas in which the coarse elastic fibers seemed to have disappeared, while the fine fibrils could still be recognized. The adventitia was of distinctly increased cellularity. The fibrocytes were swollen and often separated and mobilized. There were many mononuclear cells with a distinct rim of cytoplasm, and lymphocytes and a few oxyphilic leukocytes. In addition to these cell forms, one found elongated cells with pyknotic, crenated and elongated nuclei, which could be seen also between the muscle fibers of the adjacent portion of the media.

In the myocardium there were numerous nodular accumulations of large cells which were located near the larger blood vessels. The cells which formed the nodules had a pale-staining cytoplasm and oval nuclei with a central indented spindle of chromatin. These cells centered about areas of fibrinoid necrosis. Between them were a few lymphocytes and leukocytes. Underneath the endocardium, areas of necrosis which were surrounded by cells of histiocyte type distinctly different from the cells of myocyte type were found. In addition to the cellular nodules, there were flame-shaped scars radiating between the muscle fibers which were increased in thickness and the striations of which were obscured.

The anatomic diagnosis was coarctation of the aorta with thrombosis of the aorta distal to the coarctation; spontaneous rupture of the aorta above the aortic valve and rheumatic aortitis with necrosis of the media; verrucous endocarditis of the mitral and aortic valves and slight fibroplastic deformity of the aortic valve; slight eccentric hypertrophy of the heart; moderate dilatation of the internal mammary and intercostal arteries; chronic passive congestion of the lungs, liver, spleen and kidneys; bronchopneumonia of the right lower pulmonary lobe; bilateral hydrothorax, and follicular hyperplasia of the spleen.

CASE 2.—A white girl, aged 4 years, was brought into the Cook County Hospital on July 21, 1932. The mother stated that the child was well until two weeks before entrance when pain in the abdomen and chest, associated with vomiting, developed. It was also noticed that during the past two weeks the child had a fever. The developmental history was normal. The mother had had no miscarriages.

The physical examination revealed a well developed child acutely ill. The temperature was 103.4 F., the pulse rate 140, and the respiratory rate 26. The heart was enlarged to the left. The apex beat was displaced slightly to the left. On examination of the chest there were impairment of resonance and diminished breath sounds over the entire left pulmonary field. A friction rub was heard over

the left portion of the sternum. The temperature varied between 100 and 104 F., the pulse rate was 130, and the respiratory rate, 30. The white blood cell count was 29,400, with 78 per cent polymorphonuclear leukocytes. The roentgenogram revealed a marked cardiac enlargement, the configuration resembling a pericarditis with effusion. Aspiration of the chest yielded 100 cc. of a straw-colored fluid, the culture of which was negative. The electrocardiogram showed evidences only of a sinus tachycardia. The urine showed a trace of albumin, and microscopically there were a few pus cells, red blood cells and granular and cellular casts. The Pirquet test was negative.

The clinical diagnosis was pericarditis with effusion. A pericardial paracentesis yielded 35 cc. of a straw-colored fluid. About ten minutes later, the child became cyanotic and died five days after entrance.

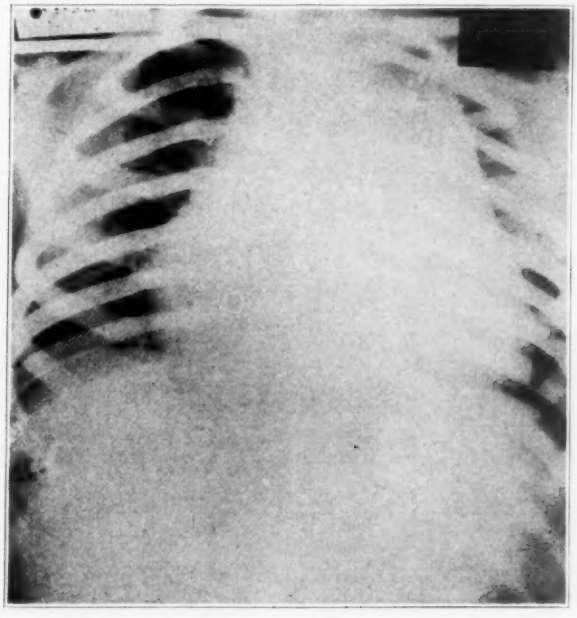

Fig. 2 (case 2).—Roentgenogram showing the large cardiac shadow with broadening, especially of the base, the configuration resembling pericarditis with effusion.

Autopsy (Dr. R. H. Jaffé and Dr. D. H. Neiman).—The pericardial sac extended from the right mamillary line to the left anterior axillary line. The sac contained 250 cc. of coagulated blood. The heart measured 70 mm. in vertical, and 50 mm. in transverse, diameter. The surface was covered by loosely adherent, granular, light pink-gray membranes. The wall of the left ventricle was 11 mm., and that of the right ventricle 5 mm., in thickness. The myocardium was light purple-pink and friable. The heart valves were grossly unchanged.

At the valve, the aorta measured 42 mm., at the diaphragm 28 mm. and at the bifurcation 18 mm. in circumference. The intima above the valve was smooth. Beyond the arch of the aorta, 8 mm. below the opening of the left subclavian artery, located in the anterior wall, was an oval opening 7 by 5 mm. in diameter.

The edges of the opening were smooth and slightly everted. The intima was smooth except for fine, pinpoint-sized granular and slightly transparent deposits near the lower edge. The opening led into a sac which was 7 cm. in vertical, 5 cm. in transverse and 5 cm. in anteroposterior diameters. The sac, which was adherent to the median aspect of the left upper pulmonary lobe, bulged into the pericardial sac, stretching its reflexed portion. The sac compressed slightly the left branch of the pulmonary artery. At the greatest convexity of the intrapericardial portion of the sac was an irregular hole 25 by 20 mm. in diameter, with indented edges. In the sac, which was lined by a whitish, finely granular membrane, was a small amount of loosely coagulated blood.

Microscopic Examination.—Approaching the opening in the descending aorta, the first change to become visible was the appearance of a layer of fibrinoid material which rested on the internal elastic membrane. This fibrinoid material contained irregular, deeply-stained and shrunken nuclei. Near the opening, the layer was raised to nodular elevations which stained brass yellow with van Gieson stain.

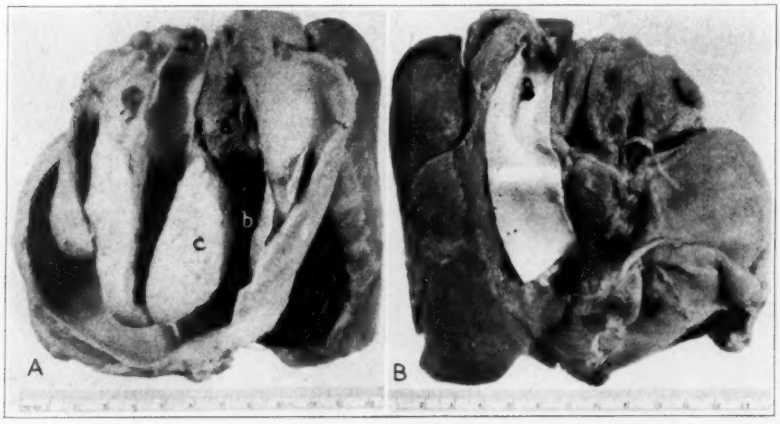

Fig. 3 (case 2).—*A*, anterior view of the heart and the aorta showing saccular aneurysm, *a*, protruding anteriorly into the dilated and thickened pericardial sac, *b*, just to the left of the ascending aorta; *c* indicates the wall of the left ventricle. *B*, posterior view of the heart and the descending aorta showing the small opening in the aorta (*a*) into the aneurysmal sac.

Here and there one found close to the internal elastic membrane a group of better preserved, oval nuclei forming small palisades with the nuclei perpendicular to the membrane. At the opening, the layer of fibrinoid necrosis bent outward to pass into the internal lining of the sac. The point of bending was marked by a greater cellularity, and besides cells with shrunken and indented nuclei, there were some lymphocytes and an occasional multinucleated giant cell. Underneath the nodular elevations, the media revealed severe changes. The muscle fibers were necrotic and hyalinized, and the chromatin granules of the broken down nuclei formed fine, dustlike precipitates. At the border of the media and adventitia, the zone of necrosis extended for some distance beyond the changes of the intima in the form of a tonguelike projection. Stains for elastin demonstrated that the internal elastic membrane was destroyed underneath the nodular formations of fibrinoid material. In the necrotic area of the media the coarser elastic fibers were

still visible, but they were broken up into small pieces and curled, and the finer fibrils had disappeared. The adventitia was well preserved and contained only an occasional small accumulation of round cells.

The wall of the aneurysm was in continuation with the wall of the aorta, the layers of which could still be recognized though they were severely changed. Innermost there was a broad band of fibrinoid necrosis with shrunken, pyknotic and broken up nuclei which corresponded to the intima and media. Immediately adjacent to the lumen, remnants of intact tissue could be detected which caused the internal lining of the sac to be smooth. These remnants consisted of a few connective tissue trabeculae with preserved fibrocyte nuclei. The connective tissue

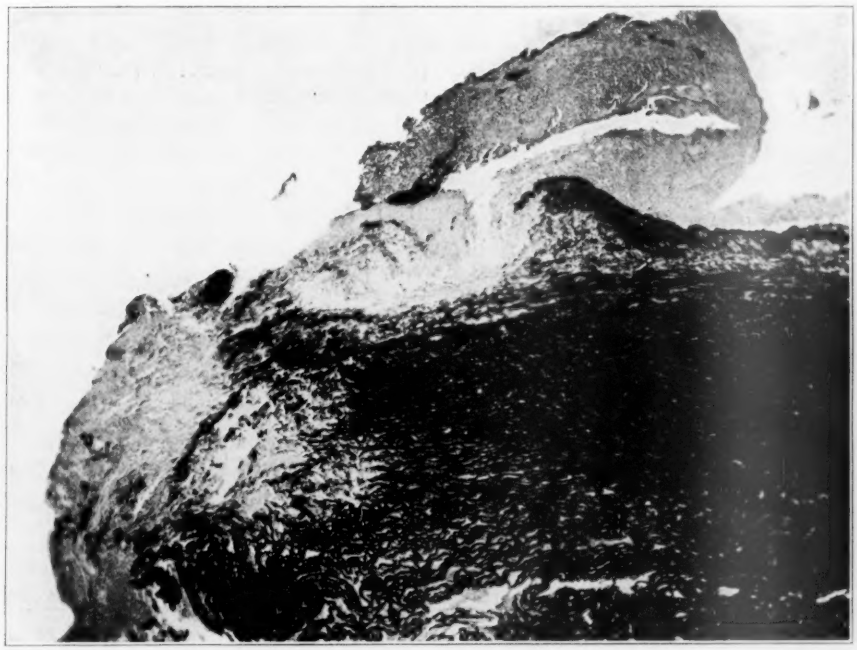

Fig. 4 (case 2).—Section taken from the aorta at the point of the rupture (elastica stain; × 150). A layer of fibrinoid material rests on the internal elastic membrane. Near the opening, the layer is raised to nodular elevations. Underneath the nodular elevations the media reveals necrotic and hyalinized muscle fibers. The internal elastic membrane is destroyed underneath the nodular formations of fibrinoid material.

soon passed into the fibrinoid necrotic material which was particularly rich in nuclear débris in the places corresponding to the media. In these places, one also found remnants of elastic tissue in the form of tortuous segments still suggesting the arrangement of the elastic tissue of the media. Near the adventitia, mononuclear cells, neutrophilic cells and a few oxyphilic leukocytes were seen between the shrunken and disintegrated nuclei of the preexistent structures.

The adventitia was the only layer which had remained intact. It was thick and formed by dense connective tissue interspersed by a moderate number of elastic fibrils. Quite a number of dilated capillary blood vessels were present

which were often surrounded by accumulations of lymphocytes, plasma cells, histiocytes and a few leukocytes. Gram-Weigert stain demonstrated single gram-positive diplococci and streptococci in the nodular elevations on the inside of the aorta. These cocci became abundant in the region of leukocytic-histiocytic infiltrations of the aneurysmal sac, where they were found also inside of mononuclear and polymorphonuclear elements. Sections taken from other portions of the aorta did not show abnormal changes.

About the blood vessels of the myocardium were small scars which radiated between the muscle fibers and contained an occasional small accumulation of myocytes.

The anatomic diagnosis was: verrucous streptococcic aortitis of the descending portion with formation of an aneurysm; perforation of the aneurysm into the pericardial sac and tamponade of the pericardial sac by the hemorrhage; compression atelectasis of the left lung and recent hemorrhagic infarct in the apex of the left lung; loose fibrous adhesions about the left lung; compensatory emphysema of the right lung; cloudy swelling and anemia of the liver; hyperplasia of the lymph follicles of the spleen; slight congestion of the kidneys and ascites and left hydrothorax.

COMMENT

The first detailed study of the histologic changes in the aorta resulting from rheumatic infections was made by Klotz [9] in 1912. Fifteen necropsies composed his series, ranging from first attacks of rheumatic fever to recurrent attacks with progressive heart disease. He observed that the aorta is damaged by the inflammatory process, which travels along the vasa vasorum, and that during the acute process there is destruction of elastic and muscle tissue, the inflammatory exudate consisting mostly of lymphoid cells. When the degenerative process is extensive, the media is weakened from the necrosis of considerable tissue. He further stated that the intima of the arteries does not appear to be primarily affected, although slight superficial fatty changes are occasionally seen early, while later intimal proliferation may give rise to nodular endarteritis.

Some years later, in 1924, Pappenheimer and Von Glahn [10] restudied this problem and elaborated on it. They expressed the belief that the distinctive lesion of the aorta is a scar, the shape of an inverted wedge, often acellular and located in the region of the vasa vasorum. In some of the cases they noted typical Aschoff cells in the adventitia with little tendency toward grouping. They admitted that invasion of the aorta by way of the lumen might occur, but considered the latter unlikely as the primary portal of entry for lack of sufficient evidence. Perla

9. Klotz, O.: Rheumatic Fever and the Arteries, Tr. A. Am. Physicians **27**:181, 1912.

10. Pappenheimer, A. M., and Von Glahn, W. C.: Lesions of the Aorta Associated with Acute Rheumatic Fever and with Chronic Cardiac Disease of Rheumatic Origin, J. M. Research **44**:489, 1924.

and Deutch [11] and Kugel and Epstein [12] concurred in this view. Many other reports have since appeared presenting histologic evidence of the damaging effects of rheumatic fever on the aorta (Weisl [13] and Besançon and Weil [14]), even severe enough to cause the formation of aneurysms (Gray and Aitken [15]). Changes in the adventitia were described by Chiari [16] and Barnard [17] as perivascular round cell accumulations and nodular fibrosis.

In spite of all these investigations, few references are made to primary verrucous lesions in the intima of the aorta in rheumatic infections, but much emphasis is placed on the primary and extensive involvement of the adventitia and media, the changes extending along the vasa vasorum, i. e., invasion by means of the vasa vasorum with involvement of the adventitia alone; more extensive inflammation leading to involvement of the media, and, lastly, even the intima. Depending on the extensiveness of the reaction, the resulting scar may vary from a microscopic wedge-shaped area all the way to a gross scar (Pappenheimer and Von Glahn [10]). Macroscopic scars may also result from involvement of the walls of the vasa vasorum with subsequent thrombosis in those vessels. These large scars are rare in rheumatic fever but, when present, show a definite histologic difference from syphilitic scars of the media (Gray and Aitken [15]). It can readily be seen that if the inflammatory, degenerative and fibrotic processes sufficiently weaken the media, formation of an aneurysm can easily result.

That the lumen of the aorta may serve as the portal of entry for the primary involvement of the intima is shown in the two cases reported here, both of which showed similar verrucous lesions on the intima of the thoracic aorta. Streptococci were present in the lesion in the second case. The genesis of the lesion is probably as follows, according to Neiman: [18] In a circumscribed area, at the point of attack of the offending agent, a fibrinoid swelling of the intima occurs which progresses

11. Perla, D., and Deutch, C. M.: The Intimal Lesions of the Aorta in Rheumatic Infection, Am. J. Path. **5**:45 (Jan.) 1929.

12. Kugel, M. A., and Epstein, E. G.: Lesions in the Pulmonary Artery and Valve Associated with Rheumatic Cardiac Disease, Arch. Path. **6**:247 (Aug.) 1928.

13. Weisl: Med. Klin. **19**:197, 1923.

14. Besançon and Weil: Lancet **1**:1002, 1928.

15. Gray, S. H., and Aitken, L.: Late Gross Lesions in the Aorta and Pulmonary Artery Following Rheumatic Fever, Arch. Path. **8**:451 (Sept.) 1929.

16. Chiari, H.: Ueber Veränderungen in der Adventitia der Aorta und ihrer Hauptäste im Gefolge von Rheumatismus, Beitr. z. path. Anat. u. z. allg. Path. **80**:336, 1928.

17. Barnard, W. G.: Diffuse and Nodular Fibrosis of the Adventitia of the Aorta (Rheumatic Periaortitis), J. Path. & Bact. **32**:1, 1929.

18. Neiman, B. H.: Personal communication to the authors.

to such an extent that it rises above the surface of the unaffected intima. Later a proliferation of the cells of the intima, chiefly fibrocytes with a varying amount of small round cells, takes place with the formation of a definite nodule. Morphologically these verrucae are similar to those occurring on the cardiac valves. The process may then either subside, leaving a plaquelike scar, or progress, the necrosis becoming prominent. The inflammatory and necrotic area may then penetrate into deeper layers, breaking through the internal elastic membrane and involving the media. This involvement may be so extensive as to cause a rupture of the aorta as was noted in the first case, in which rupture occurred without definite formation of an aneurysm, probably because of the markedly increased blood pressure proximal to the coarctation of the aorta. If not for the coarctation with the heightened blood pressure, the weakened area of the aorta might gradually have stretched and given way, with formation of an aneurysm, as in the second case, in which, with the same type of verrucous aortitis but without coarctation or hypertension, a saccular aneurysm developed, which secondarily ruptured into the pericardium.

Is the verrucous aortitis present in these two cases rheumatic in origin? According to Jaffé and Neiman,[19] in the first case the myocardium revealed nodular accumulations of large cells located near the larger blood vessels, presenting the characteristic picture of Aschoff nodules. Consequently, in the first case the aortic lesion was definitely on a rheumatic basis. In the second case there were small scars about the blood vessels of the myocardium which contained an occasional small accumulation of myocytes. These scars may have been on the basis of rheumatic fever. Streptococci were demonstrated in this case.

SUMMARY

1. The etiologic factors in all of the reported cases of thoracic aortic aneurysms in children are enumerated, with a review of the literature.

2. The etiology of thoracic aortic aneurysm in childhood and its relationship to rheumatic fever are discussed.

3. Two cases of spontaneous rupture of the thoracic aorta in children, aged 11 and 4 years, respectively, are reported; in one case, the rupture was proximal to coarctation of the aorta, diagnosed during life, and in the other the rupture was through an aneurysmal sac into the pericardium.

4. Both cases showed verrucous aortitis as the primary pathologic condition leading to the rupture.

5. The formation and extension of the lesion are discussed.

6. One case showed typical, and the other suggestive, findings of rheumatic myocarditis.

19. Jaffé, R. H., and Neiman, B. H.: Personal communication to the authors.

CUTANEOUS REACTIONS OF CHILDREN TO PNEUMOCOCCUS AND STREPTOCOCCUS VACCINES

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The solution of some problems in the pathology of the diseases of the respiratory tract can be approached only by the combined efforts of the internist and the bacteriologist-immunologist. Research on the relations between lobar and lobular pneumonia requires such a collaboration. It is usually considered that typical lobar pneumonia is very rare in infants and young children, occurring more frequently in older children and adults, while lobular pneumonia, on the contrary, is more frequent in infants and young children. The existence of a relation between the age of the patient and the type of pneumonia is evident, although its cause is not clear. As differences in immunity have often been thought responsible, the problem has been attacked by means of a study of immunologic reactions, i. e., cutaneous reactions, it being tacitly understood that both lobar and lobular pneumonia are caused by the pneumococcus. This is, however, not certain, especially with regard to the latter.[1] The fact that pneumococci are found in this condition, which usually occurs after influenza, measles, typhoid fever or some other acute disease, shows merely that these microbes have increased in number so as to maintain a secondary infection, as every healthy person harbors virulent pneumococci in the respiratory tract.

PREVIOUS INVESTIGATIONS

The antigen for the cutaneous test mentioned has been prepared in different forms by various workers: dead pneumococci in salt solution (Kramar[2]), filtrates of fluid cultures (Gutfeld and Nassau[3]), protein fractions of pneumococci, type-specific carbohydrates of pneumococci, pneumococci dissolved in bile (Herrold and Traut[4]),

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From the Children's Clinic and Hygienic Laboratory of the University of Amsterdam.

1. Vedder, A.: Pneumococcus en Pneumococcose, Amsterdam, Kinsbergen en Co., 1932.

2. Kramar: Arch. f. Kinderh. **89**:81, 1929; **91**:278, 1930; **93**:161, 1931; **94**:81, 1931.

3. Gutfeld and Nassau: Jahrb. f. Kinderh. **112**:155, 1926.

4. Herrold and Traut: J. Infect. Dis. **40**:619, 1927.

pneumococcus autolysates (Steinfield and Kolmer [5]), alcoholic extracts of pneumococci (Clough [5a]), etc. The results obtained differ widely; the same is true for the way they are interpreted, especially as to whether a positive reaction has a significance analogous with that of a positive Pirquet or Schick reaction.

The importance of this problem and the lack of agreement on it in the literature seemed to justify the enterprise of a research on the cutaneous reactions of children to pneumococcus vaccines. As vaccine a suspension of heat-killed pneumococci (one-half hour at 65 C.) was used, products of autolysis or metabolism being carefully removed by repeated washing, for these "toxic" products may cause erythema on intracutaneous injection.

METHOD

The vaccines were prepared in the following way: The wall of the pharynx of a child with lobar pneumonia, lobular pneumonia or bronchitis was swabbed with a throat swab. The swab, after inoculating a blood-agar or a blood-benzidine-agar plate, was incubated for four or five hours at 37 C. in dextrose broth. From 1 to 2 cc. of this culture was injected intraperitoneally into two mice, which died as a rule within from twenty-four to forty-eight hours. From the blood of the heart pneumococci were isolated on blood agar, and from this plate single colonies were transferred into ascites or serum broth. If the mice failed to die, single colonies were taken directly from the blood-agar plates. In this case it was uncertain whether the chosen colonies were virulent or not, as the virulent and the avirulent strains give similar colonies. After breeding for twenty-four hours the cultures were centrifugated, and the sediment was washed three times with salt solution, resuspended in salt solution and immediately afterward inactivated at 65 C. After controlling the sterility, the pneumococci per cubic centimeter were counted by the method of Wright. The suspension was diluted to from 6,000,000 to 20,000,000 pneumococci per cubic centimeter. No use was made of disinfectants (phenol, etc.), because such substances are known sometimes to affect the antigenicity of other microbes. Every strain was tested for its type specificity by means of microscopic agglutination tests.

In preparing the vaccines members of the thirty-two known types of pneumococci and of those of group x were used. Some strains did not show all the typical pneumococcic characters, but when used as vaccines they behaved in the same way as the typical strains. Therefore afterward vaccines prepared from green-producing streptococci from rabbits and hemolytic streptococci (erysipelas) were used. These vaccines and likewise those of Vibrio cholerae and Bacillus typhosus, the latter being used as a control, were obtained by the same method. This does not imply that they contain the same substances as the pneumococcus vaccine. The skin test was performed in the way described by Nassau and Gutfeld, the subject receiving in the forearm intracutaneous injections of 0.1 cc. each of several vaccines. Sterile salt solution was used as a control. At first the area of injection was examined every three hours, except at night; later readings were made only every twenty-four hours. Although the intensity of the reaction changed in the course of twenty-four hours and individual differences were noted, the more frequent readings could not be kept up for practical reasons. A study of the

5. Steinfield and Kolmer: J. Infect. Dis. **20**:344, 1912.

5a. Clough, P. W.: Bull. Johns Hopkins Hosp. **26**:37, 1915.

variations in intensity of the reaction during a certain period, in order to recognize early, late and allergic reactions, would be desirable.

The reaction was judged according to the size of the intumescence and the red area: 0 indicates negative; +, weakly positive; ++, positive; +++, strongly positive, etc.

Some vaccines gave strong reactions in most instances; others, only weak ones. Different reactions to various vaccines in the same person were noted, which should be attributed partially to technical failure of the injection, a drop of the liquid (i. e., 50 per cent) sometimes flowing back through the puncture opening. This factor, together with a certain subjectivity in the reading of the results, hampered the forming of an objective judgment.

EXPERIMENTS

The cutaneous test was made on about 300 persons, consisting of children of all ages and also adults, acting as controls. The results obtained in various groups are shown in table 1. Eighteen infants under 3 months were examined; they showed hardly any reaction. One child had lobular pneumonia; the others had diseases not connected with the respiratory tract and had not previously suffered from a disturbance of the respiratory system.

The + + reaction was obtained with a vaccine that always gave vehement reactions and is therefore of no importance. The infant recovering from lobular pneumonia gave a negative reaction. The number of children in this group is too small to draw conclusions. Only one third of the infants reacted to pneumococcus-streptococcus vaccines, and most of them very weakly. This is not due to absolute skin anergy in very young infants, for the Pirquet reaction can be positive at this age. It is possible that the differences between weakly reacting and nonreacting infants are connected with maternal immunity, breast feeding, etc.

Forty-seven infants from 3 months to 1 year were examined, and some of them showed a very intense reaction. Soon it appeared that those children had suffered some time before from a pneumococcic disease. Therefore the children were divided into two groups, one containing those who had previously suffered from pneumonia, bronchitis, severe cold and other diseases of the respiratory tract (positive anamnesis), and the other, those who had not (negative anamnesis). At this age the history as to morbidity was considered still to be reliable.

From the results obtained it appears that infants who have recovered from a pneumococcosis often give a positive reaction, while infants who have not had such an infection in the majority of cases give a negative reaction. Of the infants with a positive anamnesis, 6 reacted intensely (+ + + or + + + +). The child reacting + + + + had been ill three times with bronchitis; the five children giving a + + + reaction

had suffered from lobular pneumonia. At what time after the illness the reaction becomes positive could not be established. One is inclined to believe that a positive reaction has a significance analogous to that of a positive Pirquet reaction; at least, it points to sustained infection.

At first the older children also were divided into those with a positive and those with a negative anamnesis. This division, however, is left out here because the histories proved to be unreliable.

On closer examination it appeared that children who had suffered from lobar pneumonia and also those with a history of acute rheumatic fever or of chorea gave a negative reaction. For this reason the test

TABLE 1.—*Reactions of Children (and Controls) in General Series*

		Reaction							
		Positive						Negative	
Age Group	No. of Subjects	++++	+++	++	+	Total No.	Per Cent	No.	Per Cent
Under 3 months	18	..	..	1	5	6	33	12	67
3 months to 1 year:									
Negative anamnesis	23	..	..	1	9	10	44	13	56
Positive anamnesis	24	1	5	5	8	19	79	5	21
1 to 3 years	32	..	3	5	8	16	50	16	50
3 to 6 years	33	..	1	7	10	18	55	15	45
6 to 12 years	55	..	4	20	17	41	75	14	25
Students	20	..	1	10	5	16	80	4	20

TABLE 2.—*Reactions of Children with a History of Lobar Pneumonia, Acute Rheumatic Fever or Chorea*

		Reaction					
		Positive				Negative	
Disease	Number of Subjects	++	+	Total No.	Per Cent	No.	Per Cent
Lobar pneumonia	23	1	5	6	26	17	74
Rheumatic fever or chorea	15	1	1	2	13	13	87

was made on a greater number of children, mostly older than 5 years, who some time previously had had lobar pneumonia. The results, shown in table 2, indicate that such children evidently react much less frequently to pneumococcus-streptococcus vaccines than do other children of their age.

Further, the test was made on children who had suffered from acute rheumatic fever and chorea. In comparison with the results for other children of the same age a much higher percentage of positive reactions might have been expected than was obtained (table 2). The low incidence of positive reactions in persons who had suffered from rheumatic fever or from lobar pneumonia seems the more remarkable as these conditions have features in common. Both show a tendency to recurrence, and in both the streptococcic and the pneumococcic group of

organisms is probably of etiologic importance. It is surmized that here a negative reaction indicates a higher sensibility.

In consequence of this observation, attention was drawn to erysipelas, a third recurrent entity in which streptococci play an etiologic rôle. Data were obtained from 101 patients, mostly adults, who had been nursed during the past year at the Dr. D. Herderschee's ward for patients with infectious diseases in the Wilhelmina Hospital. Forty persons had suffered from repeated attacks, which makes an incidence of recurrence of 24 per cent. The skin test was made on these 40 persons, 26 of whom (35 per cent) had had one previous attack and 14 (7.5 per cent), three attacks.

In 101 patients the incidence of recurrence amounted to 24 per cent, and the number of negative reactions to 27 per cent. For the persons who had suffered from one attack the incidence of recurrence appeared to be 35 per cent; the skin test was negative in 38 per cent of these

TABLE 3.—*Reactions of Persons with Recurrent Erysipelas*

	Number of Subjects	Reaction				Chance of Recurrence
		Positive		Negative		
		Number	Per Cent	Number	Per Cent	
Total	40	29	72	11	27	24%
One previous attack	26	16	62	10	38	35%
Two pervious attacks	11	10	91	1	9	7.5%
Three previous attacks	3	3	100	0	0	0+%

patients. After the second attack the incidence of recurrence amounted to 7.5 per cent, while the skin test was negative in 9 per cent of the patients. Of the 3 patients who had suffered from three attacks, none gave a negative reaction. No case of a fourth attack of erysipelas was observed. So far as it is allowed to draw conclusions from this limited number, it seems that with each repeated attack the chance of further recrudescence diminishes and that the incidence of negative reactions falls in the same degree. In persons who have suffered from erysipelas a positive cutaneous reaction seems to point to immunity; a negative one indicates that recurrence may occur. Supposing this to be true, the skin test should be negative during the course of the illness. This proved to be the case. In 4 persons the test was made during the acute stage of the disease. It was negative with streptococcus and pneumococcus vaccines, while positive in 3 patients with cholera vaccine. The lack of reaction was therefore not due to absolute skin anergy.

COMMENT

Vaccines from different types of pneumococci do not show type-specific quantitative or qualitative differences and act in the same way as vaccines from atypical pneumococci and green-producing or hemolytic

streptococci. It was generally found that the skin reaction obtained with various pneumococcus and streptococcus vaccines in one person were either all negative or all positive although, as a result of the causes mentioned, they differed in intensity.

The vaccines of all members of the streptococcus-pneumococcus group behave in the same way. Therefore, the skin reaction is to be considered not as type-specific nor as species-specific but as group-specific. It is not merely a reaction to a protein or microbic vaccine, for the control tests proved that persons reacting in the same way to streptococcus-pneumococcus vaccines behaved differently to typhoid and cholera vaccines. Moreover, the cutaneous reaction of Pirquet was negative in nontuberculous children who reacted positively to streptococcus-pneumococcus vaccines. Incidentally it may be mentioned that the Pirquet reaction also is group-specific, for the differences in intensity of the reactions to human and bovine tuberculin are independent of the type of tubercle bacilli causing the infection.

Although about 300 persons have been examined with some thirty vaccines, it is felt that this number is too small for a final conclusion. Only some suggestions will be advanced, which may serve as a working hypothesis for further research.

The skin reaction is specific for the streptococcus-pneumococcus group, but without any species-specificity. It seems that after a patient has undergone a streptococcic or pneumococcic infection the skin reaction often becomes positive. In persons who have not been ill or who are at the moment still in the acute stage of such a condition the reaction is negative. From the material reported it is concluded, especially on account of the findings in patients with erysipelas, that probably some relation exists between the incidence of recurrence and a negative skin reaction. Persons in whom the reaction is positive do not contract erysipelas, lobar pneumonia or rheumatic fever, while those who give a negative reaction may contract these conditions. As a search of the literature does not reveal that a person who has suffered from lobar pneumonia is more liable to have erysipelas or rheumatic fever than another, or that patients with erysipelas contract lobar pneumonia and rheumatic fever more frequently, it follows that apart from the *group*-specific sensibility, *disease*-specific factors play a part, which cannot be registered by means of the skin test. It is therefore emphasized once more that the cutaneous reaction reveals only a sensibility for this *group* of diseases.

Possibly a relation exists between the lower frequency of lobular pneumonia in older children and the decreasing incidence of negative skin reactions. Granting this to be true, the tendency toward the development of lobular pneumonia in typhoid and pertussis can perhaps be accounted for by an aspecific loss of immunity, as according to

Kramar in pertussis the cutaneous reaction often is negative while the reaction to tuberculin—as is known—also may be negative. The same may be the case with elderly people, who more frequently contract pneumonia and tuberculosis. Apart from anatomicophysiologic causes, this might be due to loss of immunity, as would appear from a greater incidence of negative reactions.

The negative reactions in rheumatic fever and chorea favor the theory that in these conditions pneumococci and streptococci play an etiologic rôle.

If a positive skin reaction is a proof of immunity, and a negative one, of sensibility, one might try to change by vaccination a negative reaction into a positive one. In this way it would perhaps be possible to protect patients in whom after erysipelas, lobar pneumonia or rheumatic fever the reaction remains negative against a repeated attack of these conditions. For the reasons already mentioned, these vaccines should be species-specific.

As to the problem of the relation between this skin reaction and the tests of Pirquet and Mantoux, on the one hand, and those of Schick and Dick, on the other, this test seems to have a significance analogous to that of the tests of Pirquet and Mantoux: A positive reaction indicates some degree of immunity against a repeated infection. (The theory advanced by Calmette that the Pirquet test indicates merely allergy and not immunity is not accepted.)

Theoretically, it is possible that a negative skin reaction is due either to an absolute aspecific skin anergy (infants?) or to positive anergy. The rather high number of older children and adults giving a negative reaction seems to plead in favor of the latter hypohesis, according to which the allergic state is changed by repeated infections into positive anergy.

In our opinion, however, it is more probable that the negative skin reaction in adults is caused by gradual loss of immunity. Persons with a negative reaction are therefore more liable to incur pneumonia, erysipelas, etc. Apart from this sensibility many other factors are of etiologic importance in the development of these diseases, for instance, catching cold in pneumonia (van Loghem).

No answer can be given to the question why infants frequently contract lobular pneumonia but seldom lobar pneumonia, young children transitory pneumonia (Uebergangspneumonie[6]) and adults mostly lobar pneumonia. The anatomic and physiologic factors connected with age, the kind of pneumococci, etc., probably are of influence. No observations were made which suggested, as is sometimes accepted, that lobar pneumonia may be an allergic reaction.

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6. Wiskott: Zur Pathogenese, Klinik und Systematik der frühkindlichen Lungenentzündung, Berlin, S. Karger, 1932.

CONCLUSIONS

1. Infants younger than 3 months react weakly or not at all to intracutaneous injections of vaccines of dead pneumococci and streptococci.

2. Older infants and young children react in a gradually increasing percentage of cases.

3. No type-specific or species-specific differences between the vaccines were observed. Vaccines of pneumococci and green-producing and hemolytic streptococci act the same.

4. The reaction is specific for the group of pneumococci and streptococci.

5. Children who have suffered from bronchitis, lobular pneumonia and other conditions in which pneumococci and streptococci are of etiologic importance often give a positive reaction; other children, a negative reaction. Possibly as a result of such a condition a negative reaction changes into a positive one.

6. Older children and adults (students) in the majority of cases react positively.

7. Children who have suffered from lobar pneumonia, acute rheumatic fever and chorea almost never react to the vaccines.

8. In persons having suffered from erysipelas the percentage incidence of negative reactions is the same as the chance of recurrence.

9. In erysipelas a positive reaction points to immunity; a negative one indicates that a chance of recurrence exists. In lobar pneumonia and rheumatic fever also some relation perhaps exists between a negative reaction and the incidence of recrudescence.

10. The skin reaction has a significance analogous to the tests of Pirquet and Mantoux.

FAMILY PERIODIC PARALYSIS

WITH A REVIEW OF THE LITERATURE

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NEW YORK

The condition known as "family periodic paralysis," "paroxysmal paralysis" and "myoplegia periodica" was recognized as a clinical entity by Schachnowitsch [1] in 1882, but the first detailed descriptions of this disease were given by Westphal [2] and Oppenheim in 1885 and 1889, respectively. Despite the fact that their patient was a child, there are, to our knowledge, only a few reports of this disease in the pediatric literature. This is surprising since its unknown etiology and pathogenesis present many problems which are not only of neurologic but of general interest.

I have recently had the opportunity of studying a family with this disease, and two children, members of this family, were admitted to the hospital for observation. It seems worth while to present a short report of the disease as it has occurred in the patients' family and a description of its peculiarities in childhood. For further details, I refer to the extensive reviews of Taylor,[3] Oddo and Audibert,[4] Schmidt [5] and Janota and Weber,[6] to whom I am obliged for many references.

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† Dr. Ludwig Schoenthal died on June 15, 1934.

Read before the New York Academy of Medicine, Section of Pediatrics, May 11, 1933

1. Schachnowitsch: Russk. vrach **3**:537, 1882; cited by Goldflam: Ztschr. f. klin. Med. (supp.) **19**:260, 1891.

2. Westphal, C.: Ueber einen werkwürdigen Fall von periodischer Lähmung aller vier Extremitäten mit gleichzeitigem Erlöschen der elektrischen Erregbarkeit während der Lähmung, Berl. klin. Wchnschr. **22**:489, 1885.

3. Taylor, E. W.: Family Periodic Paralysis: With a Report of Cases Hitherto Published, J. Nerv. & Ment. Dis. **25**:637, 1898.

4. Oddo, C., and Audibert, V.: La paralysie périodique familiale, Arch. gén. de méd. **1**:37, 129, 284, 415 and 590, 1902.

5. Schmidt, A. K. E.: Die paroxysmale Lähmung, Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie, no. 18, Berlin, Julius Springer, 1919.

6. Janota, O., and Weber, K.: Die paroxysmale Lähmung: Eine Studie über ihre Klinik und Pathogenese, Als Beihefte zu der Abhandlungen aus der Neurologie, Sonderausgabe von dem Hefte 46d, Abhandlungen aus der Neurologie, Berlin, S. Karger, 1928.

REPORT OF CASES

Patient 1 (H 1 in chart) was first seen in November 1932, at the age of 4½ years, in the outpatient department of the New York Hospital, where her brother was treated for chronic eczema. The boy, who is 9 years old, has been free from attacks. The mother stated that the child has suffered from "spells" since she started to walk at the beginning of the second year of life. At that time the parents noticed that several times a week she could not get up from the floor or from a chair, or they found her crying in bed, unable to turn without assistance. The child's father recognized the nature of these attacks since he and several other members of his family have suffered from the same condition since early childhood. The spells of the patient occur irregularly, sometimes two or three times in a day and sometimes weeks apart; they always last from about five to fifteen minutes. Otherwise, her physical and mental development is normal. No disturbance of the sphincters is present.

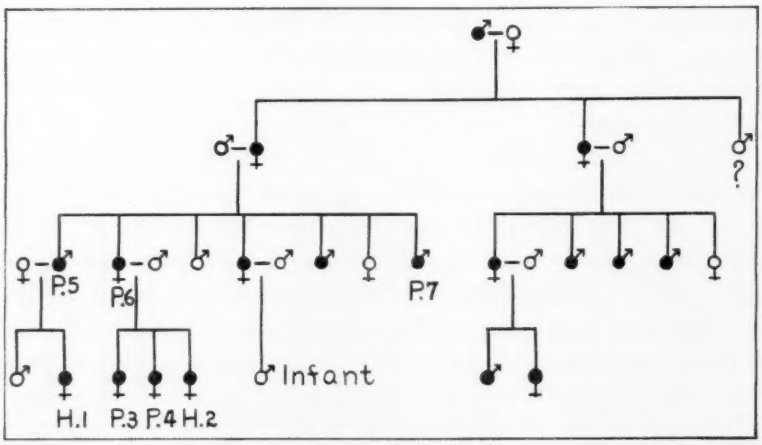

Chart showing the incidence of periodic paralysis in the family described. *P.* indicates clinic patients; *H.*, hospital patients; ♂ and ♀, normal persons; ♂ and ♀, afflicted persons; ?, condition unknown.

In the hospital, physical examination revealed a well developed, intelligent girl. Except for a questionable symmetrical hypertrophy of the calves, no pathologic condition was found. The neurologic examination (Dr. H. G. Wolff) showed nothing abnormal except a somewhat unsteady gait when the child first began to walk, which disappeared when walking continued.

One morning the child said that she felt stiff, but she was able to get up and to walk. At this time the deep reflexes in the lower extremities were absent, but the sensation was normal. The child was taken to the treatment room for determination of the electrical reactions, but by the time she arrived there the "stiffness" had disappeared and the reflexes were normal again. The attack lasted from five to ten minutes. The upper extremities were not involved. The reactions both to the galvanic and to the faradic current were tested several times while she was free from attacks, and the following results were obtained: cathodal closure contraction, 3 milliamperes; anodal closure contraction, 5 milliamperes; anodal opening contraction, 4 milliamperes, and cathodal opening con-

traction, 8 milliamperes. Since exposure to cold has induced attacks of paralysis in similar cases,[7] the right leg was immersed in water at 10 C. for thirty minutes. At the end of this time, the deep reflexes were present and equal to those of the left side. The electrical reactions remained unchanged.

Several days later the child was given physostigmine daily in increasing dosage in an attempt to precipitate an attack. Seventy-five minutes following the injection of 0.0006 Gm., the child complained of being "stiff." She was unable to walk alone. The hands and feet perspired profusely. When held up, she made incoordinate movements of the legs similar to those of a baby. The deep reflexes were absent in both extremities. The attack lasted about ten minutes. Two further injections of physostigmine at a later date were not followed by attacks.

The laboratory data were as follows: The red blood cell count was 3,840,000; the hemoglobin was 89 per cent (12 Gm. per hundred cubic centimeters); the white cell count was 8,550, with 65 per cent adult polymorphonuclears, 3 per cent immature polymorphonuclears, 28 per cent lymphocytes and 4 per cent monocytes. The urine showed rare white blood cells and no abnormal constituents. The whole blood contained[8] 80 mg. of sugar per hundred cubic centimeters, 14 mg. of urea and 0.65 mg. of creatine.

Patient 2 (H. 2 in chart), 13 years of age, a cousin of patient 1, was admitted to the hospital for study. Her mother (patient 6) and two younger sisters, aged 9 and 3 years (patients 3 and 4) suffer from the same condition. Her mental and physical development has been normal. The attacks were noticed shortly after she learned to walk and were similar to those described for patient 1. The attacks have been worse during the past year with the onset of menstruation. The menstrual periods are fairly regular and seem to have no connection with the attacks. These usually occur after relaxation following exercise, especially after a strenuous game of basketball. Recently they have come at least once daily and have lasted from about ten to forty-five minutes. The patient is a good swimmer and an all-round athlete, but her mother has restricted her activities, as she knows their effect on the attacks. Sometimes when walking home from school she "gets all out of breath" and feels very tired: "It's like having to climb a high mountain." The quantity or quality of food does not seem to affect the number or severity of the attacks. The night before admission she fell out of bed and had to be put back by her father. This had happened before. An attack is preceded by a feeling of numbness or stiffness; sometimes, warned by this "aura," the patient is able to "walk off" an approaching attack.

Physical examination revealed a well developed and well nourished girl, mature for her age. A soft systolic murmur which was not transmitted was heard over the pulmonic area. Otherwise, the physical examination gave negative results. Several attacks were observed while the patient was in the hospital. During an attack, the palms perspired profusely, although she did not perspire elsewhere. Her upper extremities were very weak but capable of slight movement. She was unable to rise from a chair or even to raise her feet from the floor. The tendon reflexes of the arms and legs could not be elicited with the exception of the triceps reflexes. Unfortunately, the electrical reactions were not determined.

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7. Neel, A. V.: Zwei von einander unabhängige Fälle von Myoplegia paroxysmatica (periodica, familiaris), Ztschr. f. d. ges. Neurol. u. Psychiat. **118**:269, 1928; Hospitalstid. **72**:48, 61, 93 and 130, 1929.

8. Benedict, S. R.: The Analysis of Whole Blood: II. The Determination of Sugar and of Saccharoids (Non-Fermentable Copper-Reducing Substances), J. Biol. Chem. **92**:141, 1932.

The red blood cells, white blood cells and differential count were normal. The urine showed rare leukocytes but no other abnormal constituents. The basal metabolic rate was minus 3.7 per cent (Aub-Du Bois standard).

The child was put on a diet free from creatine and creatinine: protein, 60 Gm.; fat, 130 Gm.; carbohydrate, 260 Gm.; total calories, 2,400 (46 calories per kilogram of body weight). On this diet the child excreted from 720 to 1,130 cc. of urine, which contained from 7.86 to 8.35 Gm. of total nitrogen, from 0.009 to 0.024 Gm. of creatine and from 0.872 to 1.026 Gm. of creatinine per twenty-four hours. She was given 1 Gm. of creatine by mouth. 39 per cent of which was excreted in the urine (calculated as creatinine), the nitrogen partition during these twenty-four hours being total nitrogen, 8.57 Gm., creatine, 0.318 Gm., and creatinine, 0.953 Gm.[9]

Since her discharge from the hospital, the child has received 0.025 Gm. of ephedrine hydrochloride twice daily, and she claims that her attacks have become less severe. We have not been able to evaluate objectively this purely subjective statement, since even without treatment the frequency and severity of the attacks are apt to vary greatly.

Patients 3 and 4 have been seen in the clinic while free from attacks. Their history and symptoms closely resemble those of their sister and cousin.

Patient 5 (the father of patient 1), 29 years of age, is a well developed man who has suffered from the same condition since early childhood. His attacks have become less severe during recent years. He was in France with the American Expeditionary Force. At that time he had frequent spells after a day's march, and whenever possible he tried to "walk them off." He was reproved for not resting and at times for not being able to arise. Finally he was sent to a psychopathic hospital under suspicion of malingering, where he was put to bed for several weeks. His condition became much worse, and following this rest period he had to learn to walk again. Physical examination at a time when he was free from attacks showed an athletically built man whose leg muscles seemed to be somewhat hypertrophic but showed no signs of weakness with the ordinary tests of muscular strength.

Patient 6 (the mother of patients 2, 3 and 4), 35 years of age, has the same condition, but the attacks have become rare and of short duration since she entered the fourth decade of life. She is a well developed woman who has never been seriously ill, but she is very reluctant about discussing this familial disease.

Patient 7 (the uncle of patients 1, 2, 3 and 4, and the brother of patients 5 and 6), a lawyer, 24 years of age, spoke freely about the condition, as he feels much handicapped by it. He has never been seriously ill. At 6 years of age, he noticed that he could not get up at 11:30 a. m. in school. If he was allowed to rise before that time, he could "walk it off." Up to his second year in the high school (at the age of 14 years) he could play baseball, but then he noticed that at times he was not able to run. When he was between 17 and 18 years old, the attacks became worse. He now "knows how to work them off." He notices that even now he is prone to have an attack after playing ball or engaging in any other kind of hard exercise, or after some excitement, such as playing cards. He has never noticed a bad effect from alcohol or sexual excitement, but he expects an attack after staying up all night. Constipation seems to favor the occurrence of attacks. He thinks that he is more likely to have an attack if he does not eat.

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9. Dr. E. Shorr and Dr. H. G. Wolff gave valuable advice and assistance during the metabolic study.

At the onset of a spell he has a feeling of stiffness. He is usually completely paralyzed for one hour, but sometimes an attack lasts for from twenty-four to forty-eight hours. Such an attack occurs especially after he has "walked off" several attacks. He has had seizures of from one to two days' duration when he walked "without muscles;" when given a little push he would fall over. Sometimes the vision gets blurred during an attack. He has never felt any respiratory embarrassment or difficulty in swallowing.

Physical examination showed a well developed young man. The only abnormal finding was a weak grip of both hands, but all reflexes were present at that time (11:00 a. m.). The patient told us that he would take a walk and return in an attack. At 6:00 p. m., he returned. After lying down for fifteen minutes, he could hardly stand on his feet. Profuse sweating of the hands and feet was noticed. The palms were markedly red. He was asked to get a piece of paper from the floor, and he did it by climbing up on his body like a patient suffering from muscular dystrophy. At that time, he told us that vision was blurred, although examination of the eyes did not reveal any objective signs. The tendon reflexes of the arms were weak but present. Those of the lower extremities were absent. The grip of the hands and the kick of the feet were very weak. When he closed his eyes he could not stand alone (Romberg sign). There was no myotonic reaction of the muscles on mechanical stimulation. The paralysis lasted for about fifteen minutes, and then the function of the muscles slowly returned to normal, beginning in the upper extremities. Electrical reactions were not determined.

COMMENT

The histories and results of physical examinations of these patients contain most of the important manifestations of familial periodic paralysis: attacks of flaccid paralysis with loss of mechanical and electrical irritability of the muscles, without sensory or psychic disturbance, beginning in the first decades of life and occurring at irregular intervals (being more frequent and of longer duration after puberty and decreasing in number and severity after the third decade of life), usually in many generations of a family.

The hereditary nature of the condition is obvious in the family described, as it is in about 80 per cent of all cases [5] which have been reported.[10] In many families, as in ours, the disease is transmitted

10. (*a*) Buzzard, E. F.: Three Cases of Family Periodic Paralysis, with a Consideration of the Pathology of the Disease, Lancet **2**:1564, 1901. (*b*) Cousot, J.: Un cas de paralysie périodique, Rev. de méd. **7**:190, 1887. (*c*) Crafts, L. M.: A Fifth Case of Family Periodic Paralysis, Am. J. M. Sc. **119**:651, 1900. (*d*) Davis, D. B., and Wells, S. M.: Familial Periodic Paralysis: Report of a Case, J. Nerv. & Ment. Dis. **75**:160, 1932. (*e*) Favill, J., and Rennick, C. F.: A Case of Family Periodic Paralysis, Arch. Neurol. & Psychiat. **11**:674, 1924. (*f*) Gatti, M. L.: La paralysie périodique, Gaz. d. hôp. **84**:1327, 1911. (*g*) Goldflam, S.: Ueber eine eigentümliche Form von periodischer familiärer, wahrscheinlich autointoxikatorischer Paralyse, Wien. med. Presse **31**:1418, 1458, 1499 and 1535, 1890; (*h*) Ueber eine eigentümliche Form von periodischer familiärer, wahrscheinlich autointoxikatorischer Paralyse, Ztschr. f. klin. med. (supp.) **19**: 240, 1891; (*i*) Weitere Mitteilung über die paroxysmale, familiäre Lähmung, Deutsche Ztschr. f. Nervenh. **7**:1, 1895; (*j*) Dritte Mitteilung über die paroxys-

(Footnote continued on next page)

directly from generation to generation (dominant type of inheritance); in others one or more generations may apparently be free from the disease (recessive type of inheritance). In a number of typical cases, however, only one member of the family is known to have suffered from the condition.[11] It is questionable whether some of the sporadic cases

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male familiäre Lähmung, ibid. **11**:242, 1897. (*k*) Heveroch, A., cited by Janota and Weber.[6] (*l*) Hirsch, K.: Ueber einen Fall von periodischer familiärer Paralyse, Deutsche med. Wchnschr. **32**:646, 1894. (*m*) Holtzapple, J. E.: Periodic Paralysis, J. A. M. A. **45**:1224 (Oct. 21) 1905. (*n*) Kulneff, N.: Myatonia periodica, Nord. med. Ark. **2**:1 and 21, 1902. (*o*) Maclachlan, T. K.: Familial Periodic Paralysis: A Description of Six Cases Occurring in Three Generations of One Family, Brain **55**:47, 1932. (*p*) Mankowsky, B. N.: Ueber die paroxysmale Paralyse, Arch. f. Psychiat. **87**:280, 1928. (*q*) Mitchell, J. K.: A Study of a Case of Family Periodic Paralysis, Am. J. M. Sc. **118**:513, 1899. Mitchell, J. K.; Flexner, S., and Edsall, L.: A Brief Report of the Clinical, Physiological and Chemical Study of Three Cases of Family Periodic Paralysis, Brain **25**:109, 1902. (*r*) Neustaedter, M. A.: A Case of Family Periodic Paralysis, New York State J. Med. **32**:65, 1922. (*s*) Nonne: Demonstration of a Case with Family Periodic Paralysis, abstr., München. med. Wchnschr. **69**:571, 1922. (*t*) Serko, A.: Ein Fall von familiärer periodischer Lähmung, Wien. klin. Wchnschr. **32**:1138, 1919. (*u*) Wexberg, E.: Eine neue Familie mit periodischer Lähmung, Jahrb. f. Psychiat. u. Neurol. **37**:108, 1927. (*v*) Zabriskie, E. J., and Frantz, A. M.: Familial Periodic Paralysis, Bull. Neurol. Inst. New York **2**:57, 1932.

11. (*a*) Burr, C. W.: Periodic Paralysis with the Report of a Case, Pacific Rec. **8**:24, 1893. (*b*) Donath, J.: Ein Fall von traumatischer periodischer Lähmung, Wien. klin. Wchnschr. **13**:37, 1900. (*c*) Fuchs, A.: Demonstration eines Falles von periodischer Extremitätenlähmung, ibid. **18**:2, 1905. (*d*) Gardner, H. W.: A Case of Periodic Paralysis, Brain **35**:243, 1912-1913. (*e*) Greidenberg, B.: Ein Fall von periodischer spinaler Lähmung, Russk. vrach, 1887, p. 930; abstr., Neurol. Zentralbl. **7**:54, 1888. (*f*) Hartwig, H.: Ueber einen Fall von intermittierender Paralysis spinalis, Centralbl. f. d. med. Wissensch. **13**:428, 1875. (*g*) Infeld, M.: Ein Fall von periodischer Paralyse, Wien. klin. Wchnschr. **18**: 327, 1905. Schlesinger, H.: Ueber die periodisch auftretende (paroxysmale) Lähmung, ibid. **18**:323, 1905. (Infeld and Schlesinger reported the same case.) (*h*) Kastan, M.: Ueber einige allgemein als familiär bekannte Nervenkrankheiten (Paramyatonie, ihre Kombination mit Dystrophie, periodische Lähmung), Arch. f. Psychiat. **63**:361, 1921. (*i*) Kaufmann: Bericht über einen Fall von periodischer Lähmung, Ztschr. f. d. ges. Neurol. u. Psychiat. **22**:183, 1920. (*j*) Mailhouse, M.: Family Periodic Paralysis, Proc. Connecticut M. Soc., 1908, p. 263. (*k*) Mankowsky, B. N.: Ueber die paroxysmale Paralyse, Arch. f. Psychiat. **87**:280, 1929, case 8. (*l*) Pulawsky, A.: La paralysie totale des quatre extrémités et du tronc durant 48 heures, Gaz. hebd. de méd. **27**:570, 1890. (*m*) Putnam, J. J.: A Case of Family Periodic Paralysis, Am. J. M. Sc. **119**:160, 1900. (*n*) Samuelsohn: Ein Fall von intermittierender Paraplegie, Berl. klin. Wchnschr. **14**:607, 1877. (*o*) Singer, H. D., and Goodbody, F. W.: A Case of Family Periodic Paralysis with a Critical Digest of the Literature, Brain **24**:257, 1901. (*p*) Strauss, H.: Zur Kasuistik der paroxysmalen Lähmung, Deutsche med. Wchnschr. **58**:1408, 1932. (*q*) Sugar, M.: Ueber einen Fall von nicht hysterischer periodischer Lähmung, Wien. klin. Wchnschr. **23**:1643, 1910.

really belong in the group of periodic paralysis, since they differ in other respects from the familial type.[12]

In most families, the males are more frequently afflicted than the females,[5] but in the family described here the distribution between the sexes is about equal.

It is interesting that the disease varies in different families in the mode of transmission, time of onset, severity and frequency of attacks, and prognosis, but that the type seems to be more or less constant for the stricken members of the same family. The hereditary nature of the disease is corroborated by the fact that members of these families may suffer from other familial conditions, such as migraine [10m] or anomalies of growth.[10b] Two members of the family under consideration are said to suffer from severe attacks of headaches (patient 6 and her mother), but thus far the younger members seem to be free from this condition.

The most striking peculiarity of the disease in this family is the onset in the early years of life. In most of the patients the attacks were first noticed shortly after they learned to walk. The literature contains a number of reports in which the onset was recorded early in life. Buzzard [10a] described a family in which the mother and her two sons had spells from the time they were first able to move. Kulneff [10n] reported the occurrence of the disease in a Swedish family in which, as in our patients, the disease was recognized as soon as the children were able to stand, and especially when they started to walk. Goldflam [10g] mentioned that five members of one family on which he reported were said to have died from attacks of paralysis between the ages of 1½ and 8 years. Recently, Strauss [11p] described a sporadic case in which the attacks started with a febrile disease (encephalitis?) at the age of 2½ years. At their onset, these attacks were accompanied by fever, resembling the cases [14] reported in the literature prior to Westphal's publication.

The occurrence of the attacks in early life is rare. In a larger number of the reported cases the attacks started between the ages of 4 and

12. Bornstein, M.: Asthenia paroxysmalis, Neurol. Zentralbl. **24**:696 and 750, 1905. Bremer, L.: Intermittent Hysterical (?) Paralysis, Alienist & Neurologist **13**:326, 1892. Cramer, W. W.: J. neuropat. i psikhiat., 1908, vol. 8; abstr., Neurol. Centralbl. **28**:918, 1909. Fischl, J.: Ueber einen Fall von periodisch auftretender Lähmung der unteren Extremitäten, Prag. med. Wchnschr. **10**:401, 1885.

Footnote 13 deleted.

14. (*a*) Seiler: Periodische Lähmung, Arch. f. med. Erfahr. **1**:117, 1815. (*b*) Bataille: Observation de paralysie intermittente, Ann. de méd. physiol., 1829, vol. 16. (*c*) Cavaré: Observation d'une paralysie générale du sentiment et du mouvement affectant le type intermittent, Gaz. méd. de Toulouse, no. 38, 1853. (*d*) Romberg, M. H.: Lehrbuch der Nervenkrankheiten des Menschen, Prague, 1857, p. 752. (*e*) Gibney, V. P.: Intermittent Spinal Paralysis of Malarial Origin, Am. J. Neurol. & Psychiat. **1**:1, 1882. (*f*) Suckling, C. W.: Malarial Paraplegia, Brain **10**:474, 1888. (References *a*, *b*, *c* and *d* are quoted from Schmidt.[5])

10 years. In the majority of cases, however, the first attacks were observed during the second decade of life, especially around puberty. In a few cases the disease did not have its onset until late in life.[10g]

Evidently the severity of the attacks varies with age. As a rule, the attacks are most severe between the ages of 15 and 25 years, as in patient 7; after the end of the third decade, the attacks become less severe and less frequent (patients 5 and 6), and they may disappear later in life. This cycle of the disease during life is one of the many problems which cannot be solved until more is known about the pathogenesis.

A description of several attacks in different members of our family has been given. Some patients are able to predict an attack for a certain day or a certain hour of the day,[10g] since they know the periodic nature of the attacks; e. g., some patients have their attacks on Monday,[10u] which they ascribe to the rest and heavy food taken on Sunday. In other patients, the attacks occur irregularly, coming on most frequently during the night. They are perfectly well when they go to bed and wake up at night or the next morning completely paralyzed. Others are able to bring about an attack seemingly at will by relaxation after vigorous exercise (patient 7). The latter fact is of practical importance, since several authors (Goldflam,[10l] Greidenberg [11e]) have described the condition in soldiers (patient 5) who were threatened with court martial because the nature of their attacks coming on after physical exertion was not recognized. Various other factors, such as exposure to cold,[7] overeating of certain types of food (carbohydrate [15]) and emotional upsets, e. g., sexual excitement, have been recorded as inducing the paralysis, but, as in all chronic paroxysmal diseases, it is difficult to evaluate their significance. It seems, however, that in some cases (Neel,[7] Zabriskie and Frantz [10v]) exposure to cold will regularly produce an attack, whereas heat has the opposite effect.

It is difficult to detect prodromal symptoms in children, but in some of the adults a definite aura consisting of paresthesias, fatigue, perspiration and a feeling of fear [11q] seems to exist. The older girl whom we observed in the hospital (patient 2) stated that she frequently "felt tired before the onset of the paralysis and felt like doing things after it was over."

The complete attacks, lasting from a very short time to from forty-eight to seventy-two hours, may represent motor paralysis of almost all the striated muscles. All degrees of intensity are possible. In some patients no muscle except the diaphragm seems to be spared; the patients

15. (*a*) Yoshimura, K.: Experimental Studies on the Nature of Oversupply of Carbohydrates as the Causal Factor for the Fit of Paralysis, abstr., Jap. M. World **5**:44, 1925. (*b*) Shinosaki, T.: Klinische Studien über die periodische Extremitätenlähmung, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:564, 1926.

are greatly prostrated and hardly able to speak, to breathe or to cough, although generally the muscles innervated by the cranial nerves are much less affected. Fortunately, these severe attacks are relatively rare. In some patients, as in ours, the paralysis involves chiefly the extremities; however, patients 3 and 7 complain of shortness of breath and blurring of vision, which seems to indicate a partial paralysis of the intercostal and extrabulbar eye muscles. The speech has not been affected in any of our patients, but Janota and Weber [6] and others observed slurring of speech. One of our patients (patient 2) has difficulty in swallowing if an attack comes on during a meal, which may be due to paralysis of the muscles of the soft palate or of those of the pharynx. During the attack the patients are fully conscious and very uncomfortable because of the immobilization of the body, since the sensation is not disturbed.

The paralysis may start in any part of the body, but usually it begins in the muscles of the hips and shoulders and spreads to the periphery. Most frequently, however, the lower extremities are chiefly involved; this holds true for all of the members of the family described here. It was mentioned in the case reports that it is possible for a patient to "walk off" an attack, and it is interesting that in one of Cousot's [10b] patients, a violinist, the paralysis would attack all extremities save the arm which handled the bow. The onset of the paralysis may be accompanied by perspiration, especially of the palms and soles, which show a striking reddening at this time. Some patients vomited regularly at the beginning of an attack.

The paralysis may disappear as suddenly as it started. Usually motion returns first in the extremity which was paralyzed last. It is amazing to see a patient run around who was not able to raise his foot ten or fifteen minutes previously.

In childhood, and especially in infancy, the attacks are frequently of short duration, chiefly involving the lower extremities (abortive type). Our youngest patient stated that she felt "stiff," and on examination the tendon reflexes of the lower extremities could not be elicited. Buzzard [10a] described his patient's recollection of her paretic seizures in early childhood in a Victorian home: "When she had fallen on the floor and remained there in opposition to all nursery laws of decorum, a procedure which used not unnaturally to evoke a severe reprimand from the local authorities . . ." who did not recognize the cause of her "misbehaviour." In Kulneff's [10n] family, the child observed fell down when the paralysis occurred as soon as he started to walk and remained helpless until he was raised from the floor. At the age of 5 years he had learned to look for support and fell only rarely. In school the paralysis may cause embarrassment when the pupil is called on by the teacher and is unable to get up, and later when during games

of baseball or basketball he is unable to run. One of our patients, a strong girl, was thrown downstairs by her friends when running along with them. Since the attacks frequently come on during the night, it seems to be important to stress this type of attacks in children. The patients wake up and start to cry as they are unable to turn around; they are unable to explain what is wrong, and such crying spells during the night may go unrecognized for some time unless the parents are familiar with the condition. A more serious aspect of the attacks at night is evident from the history of patient 2, who fell from the bed several times so that finally her mother consented to have her hospitalized. It is evident from my case reports and those of others that the attacks become of longer duration during the second and third decades of life, but attacks lasting from twenty-four to forty-eight hours may occur during the first decade, as in the first case described by Westphal.[2]

The two outstanding neurologic symptoms apart from the paralysis are the disappearance of the tendon reflexes and the loss of faradic and galvanic irritability of the muscles. It is readily understood that Westphal[2] was suspicious of his electrical apparatus when he discovered the striking loss of electrical response, but all quantitative variations of the electrical reactions, including the complete failure of the muscles to react to the strongest current applied to nerve and muscle (cadaver reaction) have been observed so frequently that there can be no doubt about the pathognomonic significance of the loss of response in familial periodic paralysis.[16] For technical reasons, we were unable to determine the reactions during an attack. In the interval between attacks, the electrical reactions of one of our patients to the galvanic current were found to deviate from normal, since the anodal opening contraction was found to be less than the anodal closing contraction. This observation is in agreement with that of other investigators who have found that variations from normal seem to persist in the interval.[10g] In the majority of cases, however, the electrical reactions seem to be normal between attacks. The electrical reactions usually parallel the response to mechanical stimulation, as shown by the tendon reflexes and by direct mechanical irritation of the muscles. Both mechanical irritability of the muscle and response to electrical stimulation coincide with the paralysis and reappear with the return of power and motion in the muscles.

Other symptoms chiefly due to paralysis of striated muscles are constipation and urinary retention. In some of the cases catheterization was necessary to remove urine, though no paralysis of the sphincters of the bladder or anus has been observed in true cases of periodic paralysis. The "retention" of urine and feces is probably due to extrarenal

16. Oddo and Darcourt: Les réactions électriques dans la paralysie familiale périodique, Arch. d'électric. méd. expér. et clin. **10**:1, 1902. Donath, J., and Lukaecs, H.: L'excitabilité électrique des nerfs et des muscles curarisés, ibid. **9**:171, 1901.

and parenteral factors, such as the loss of water by perspiration, insufficient intake of water during an attack of long duration and, mainly, the failure of the auxiliary muscles of defecation and urination.

Signs of involvement of the cardiac muscle during an attack, such as transitory dilatation of the heart, systolic murmurs and changes in the electrocardiogram, have been reported by several observers.[17] In some of the fatal cases death has been attributed to acute dilatation of the heart in the absence of any other positive organic lesion (Holtzapple,[10m] Schmidt [5]). The nature of the changes in the cardiac muscle which bring about these transitory manifestations remains obscure.

The involvement of the auxiliary muscles of respiration and deglutition also seems to be of serious significance, since respiratory failure has been given as a possible cause of the death of patients who have expired during an attack (Neel,[7] Machlachlan [10o]). Patient 2 complained of shortness of breath during some of her attacks. It is surprising, in view of the inability of a number of these patients to take a deep breath, to cough, to expectorate and to swallow during attacks, that the deaths reported as due to respiratory failure are so infrequent.

The examination of the body fluids and excreta seemed to be of special interest, since it was thought that it might not only be of diagnostic significance but throw light on the nature of the condition. The results, however, were disappointing. Frequent studies of the morphologic characteristics of the blood did not reveal any significant and constant variation from normal. Equally disappointing were the results of quantitative chemical examinations of the serum, whole blood, spinal fluid and gastric juice. Recently, Zabriskie and Frantz [10v] analyzed these fluids in a typical case with modern technic and found no variation from normal. The variations of the blood sugar and those of the blood sugar curve after the ingestion of dextrose [6] should be evaluated with considerable caution, especially in sporadic cases,[15b] since normal persons and those with diseased thyroid glands may show similar fluctuations of the dextrose level. The high figures for serum calcium obtained by some investigators [10o] have not been confirmed by recent workers using more modern methods.[18] Yoshimura's finding [15a] of an increase in the content of magnesium in the serum in the presence of a normal calcium content must await confirmation in typical familial cases by other workers before conclusions as to its significance can be drawn. The search for toxic substances in the blood and urine has failed to give positive results,[19] though many observers have found indicanuria during periods of paralysis. Considering the retention of feces during the attacks, the appearance of indican may be a consequence rather than a cause of the paralysis.

17. Footnotes 2; 6; 10, *g*, *l* and *s*; 11, *c*.
18. Footnotes 6; 7; 10, *m* and *s*.
19. Footnotes 10, *c*, *g*, *i* and *q*; 11, *o*.

During the intervals, the basal metabolic rate of these patients has been found to be normal,[10o] as in one of our patients, and during an attack of paralysis [10v] the rate has been found to be unaltered. A careful study of the urinary volume and creatinine output of a patient on a purine-free diet over a period of one and one-half months was made by Zabriskie and Frantz.[10v] They found an unusual variation of the excretion of creatinine by the kidneys (from 0.5 to 2.5 Gm. in twenty-four hours). The variations in the excretion of urine were equally remarkable, but they did not take into consideration the fluid lost through the skin and lungs. There was, however, in their opinion, no clearcut relationship between the attacks and the output of urinary water and creatinine. A more detailed study of various other constituents of the urine in Zabriskie and Frantz' case did not yield any further results. In one of our patients (patient 2), the urinary volume and creatinine excretion observed during one week on a creatine-free diet showed only slight variation. The difference between our observations and those of Zabriskie and Frantz may be due to the fact that their patient suffered from much more severe and frequent attacks than our patient. Our patient when given creatine by mouth excreted it as efficiently as a healthy girl of equal age on the same diet.

Since the study of the blood and of the excreta failed to give satisfactory results, morphologic and chemical examinations of the muscles have been made in a great number of cases. Various histologic changes of the muscles, such as vacuolation of fibers and the accumulation of a granular substance, have been observed,[10j] but no one seems to have been able to evaluate the significance of these changes. According to Goldflam, similar changes have been observed in myotonia congenita (Thomsen's disease). Recently, Victor and Wolf compared the oxygen consumption of pieces of excised paralyzed and apparently normal muscle (gastrocnemius) from a patient with this disease (Zabriskie and Frantz [10v]) one of whose legs was immersed in cold water (from 11 to 15 C.). They compared the results with those obtained on a volunteer subject under identical conditions. Whereas the cooled or paralyzed piece of muscle consumed an average of 2.62 cubic millimeters of oxygen per gram per minute, the untreated muscle consumed 5.3 cubic millimeters, and the two specimens from the normal subject consumed 9.1 and 8.4 cubic millimeters, respectively. The authors believe that these results should be confirmed by other investigators before conclusions are drawn from them. The same pieces of muscle were analyzed for total, inorganic and organic acid-soluble phosphorus, phosphocreatine and creatine.[20] The content of these substances was found to be considerably lower in the patient's muscle than in that of the control, except that

20. Brandt, E., and Harris, M. H.: Phosphorus Metabolism in Muscular Disease, J. Biol. Chem. **62**:97, 1932. Zabriskie and Frantz (footnote 10 *v*).

phosphocreatine was only slightly increased. There was, however, no difference between the paralyzed and the nonparalyzed muscle of the patient. These observations are significant, but they await confirmation by other investigators before they can be accepted as a general finding in family periodic paralysis.

The results obtained by autopsies are much less satisfactory than those just mentioned. They have merely added the negative evidence that the central nervous system fails to reveal any changes. In some of the cases death was attributed to dilatation of the heart (Schmidt,[5] Holtzapple[10j]); in others it was probably the result of suffocation and aspiration due to failure of the respiratory muscles with secondary involvement of the lungs (Neel,[7] Machlachlan[10o]). Shinosaki[15b] gave an anatomic report for one of his patients, who showed no histologic changes in the muscles but definite exophthalmic goiter and an increase of the *Hauptzellen* of the parathyroid glands. He speculated on the possible hyperfunction of the thyroid and parathyroid glands in periodic paralysis, but many more autopsy reports would be necessary to associate family periodic paralysis with a dysfunction of the parathyroids. There is no doubt that there are cases of enlargement of the thyroid gland and exophthalmic goiter[21] in which attacks of periodic paralysis occur and in which treatment of the diseased gland results in mitigation of the attacks.[22]

Two groups of diseases seem to show a relation to family periodic paralysis: The first is that of hereditary myopathies, such as progressive muscular dystrophy, myotonia congenita (Thomsen's disease) and myasthenia gravis. A few cases have been described in which symptoms of one of these diseases appeared in patients with periodic paralysis.[23] The other group, which is characterized by its paroxysmal character, is the migraine-epilepsy group; examples of this association are the interesting cases described by Holtzapple,[10j] MacLachlan,[10l] Higier,[24] Gardner,[11d] Schachnowitsch[1] and Bornstein.[25] Two members of the family

21. Maclaire, A. J.: Case of Periodic Paralysis Associated with Thyroid Enlargement, J. Nerv. & Ment. Dis. **61**:44, 1925. Rosenfeld, M.: Akute aufsteigende Lähmung bei Morbus Basedow, Berl. klin. Wchnschr. **39**:538, 1902.

22. Morrison, J., and Levy, M.: Thyroid Factor in Family Periodic Paralysis: Report of Case, Arch. Neurol & Psychiat. **28**:386 (Aug.) 1932. Dunlap, A. F., and Kepler, E. J.: Occurrence of Periodic Paralysis in the Course of Exophthalmic Goiter, Proc. Staff Meet., Mayo Clin. **6**:272, 1931. Shinosaki (footnote 15, *b*).

23. Bernhardt, M.: Notiz über die familiäre Form der Dystrophia musculorum progressiva und deren Combination mit periodisch auftretender paroxysmaler Lähmung, Deutsche Ztschr. f. Nervenh. **8**:111, 1896. Westphal (footnote 2). Taylor (footnote 3).

24. Higier, H.: Zur Pathogenese der motorisch-paralytischen Aequivalente des epileptischen Anfalls, Deutsche Ztschr. f. Nervenh. **14**:325, 1898.

25. Bornstein, M.: Über die paroxysmale Lähmung (Versuch einer Theorie), Deutsche Ztschr. f. Nervenh. **35**:407, 1908.

described here suffer from periodic headache. One might think of some other rare paroxysmal disease, such as narcolepsy or cataplexy, but no cases have been described which reveal a more than superficial similarity between these conditions and periodic paralysis.[11g]

There is only one serious condition for which an attack of periodic paralysis may be mistaken, namely, Landry's ascending paralysis. Goldflam [10j] described a sporadic case in a young girl in which he made a tentative diagnosis of paroxysmal paralysis but the rapid progress and fatal outcome convinced him that he was wrong.

The clinical observations mentioned are not sufficient to explain the etiology and pathogenesis of familial periodic paralysis. It is known that the disease is hereditary in the majority of cases, and it has been assumed that there is a defect in the muscles, anatomic, chemical or neurologic, which predisposes to the attacks. A lesion of the muscle alone can explain the "cadaver reaction" which has been described. The histologic changes observed by many investigators seem to be of more than accidental significance. The chemical analysis of the muscles and the metabolic study of the patient observed by Zabriskie and Frantz seem to point to a chemical defect in the muscle. In addition to the defective muscle unit, however, it seemed necessary to assume a lability of the vegetative nervous system [26] which under certain conditions, such as fright, cold and rest after exercise, will precipitate an attack. Some of the symptoms preceding or accompanying an attack, such as perspiration, anomalies of the pulse and vomiting, have been attributed to a disturbance in the sympathetic-parasympathetic nervous system. The presence of a poison or toxin has been postulated, but no convincing evidence for its existence is available.[27] Janota and Weber [6] mentioned the analogy with other paroxysmal diseases occurring chiefly at night in which there is evidence of a participation of the vegetative nervous system, such as migraine and angina pectoris. On the other hand, there are close interrelationships of the vegetative nervous system, the vegetative centers in the midbrain and the glands of internal secretion. This may explain the occurrence of attacks of periodic paralysis in some of the patients with sporadic cases who suffer from exophthalmic goiter [15b] and in patients with organic brain lesions.[11g] It seems that progress toward a satisfactory explanation of the attacks will be possible only when more data on the chemical and morphologic composition of the muscles in cases of familial periodic paralysis are available and when, in suitable cases with infrequent but lengthy attacks, thorough studies of metabolism are made. Careful autopsy reports in sporadic cases, including histologic studies of the midbrain, may be of valuable assistance.

26. Footnotes 5; 6; 10, *o* and *p*.

27. Footnote 10, *c*, *g*, *i*, *q* and *r*.

Except for the sporadic cases mentioned, the therapy of familial periodic paralysis is purely symptomatic. In the cases in which dietary indiscretions seem to produce an attack, supervision of the diet seems to be indicated, and excessive ingestion of carbohydrate should be avoided. The recent investigation of the effect of certain amino-acids on patients with progressive muscular dystrophy may yield evidence for the dietary treatment of patients suffering from periodic paralysis.[28] It seems advisable to give these children a moderate amount of exercise without treating them as invalids, as one would treat a diabetic child. Usually the patients know under what conditions they are relatively free from attacks. The drugs which are generally used for epilepsy and migraine have failed to give consistent results. Equally unsuccessful have been all attempts to influence the disease by injection of alkaloids or of extracts from the glands of internal secretion which influence the vegetative nervous system.

The choice of a profession should be wisely guided so that discouraging changes are unnecessary. An explanation of the hereditary nature of the condition should be given to the older boy or girl so that he knows that the disease may be transmitted to the next generation.

Considering the great number of cases reported in some families, the prognosis as far as life is concerned seems to be favorable. In some families, as in the one described here, no member is known to have died from the disease, and most of them reach an old age. In others, such as Holtzapple's [10m] and Goldflam's [101] families, several members have died during an attack of paralysis. Since the diseases of childhood which affect the respiratory tract usually occur before the tenth year, it is not astonishing that none of the patients is known to have succumbed to pertussis or measles. In older persons, however, severe infections of the respiratory tract may become a danger to life. As far as the severity and duration of the attacks are concerned, a fairly accurate prognosis can be given according to the general tendency of the disease in the stricken family.

In this review of the literature no attempt has been made to evolve a new theory concerning the etiology and pathogenesis of family periodic paralysis, the chief purpose being to emphasize the clinical peculiarities of this condition as it occurs in early life. The onset in childhood is not uncommon, and in view of the absence of similar reports in the pediatric literature, it seemed well worth while to describe a family in which the seizures began before puberty in eighteen of the members.

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28. Brand, E., and Harris, M. M.: Further Studies on the Administration of Glycine in Muscular and Neuromuscular Diseases, J. Biol. Chem. **20**:100, 1933. Milhorat, A. T.; Techner, F., and Thomas, K.: Significance of Creatine in Progressive Muscular Dystrophy and Treatment of This Disease with Glycine, Proc. Soc. Exper. Biol. & Med. **29**:609, 1932.

REPEATED SEDIMENTATION TESTS

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The literature on the erythrocytic sedimentation test is rapidly becoming voluminous. Many writers have praised the test; some have condemned it; but the majority believe it has merit. Like all new tests, it probably has been overrated, and is now settling into its proper place, that of a laboratory test of real value, but one to be used only as an aid in diagnosis and not as a substitute for clinical alertness and care.

Advanced first as a laboratory procedure by Fåhraeus,[1] in 1918, as a test for pregnancy, it was soon disproved as a specific test for that condition, but other uses were found for it. It was observed that in any condition characterized by the destruction of tissue the normal rate of erythrocytic sedimentation was increased, and because of developments in this observation it has a definite use in differential diagnosis. In addition, because the rate changes early in conditions characterized by the destruction of tissue it is a valuable aid in the early diagnosis of such conditions, notably tuberculosis.

REVIEW OF THE LITERATURE

A review of the literature reveals many articles on the clinical application of the sedimentation test, while a much smaller number deals with the factors causing the changed rate which is sometimes found. Many influencing factors have been studied and offered as the causative element. The truth probably lies on middle ground. There are several factors operating at once, or these several factors may tend to support each other by their physiochemical relation.

Fåhraeus and Hoeber [2] were of the opinion that an increased rate was caused by an increased tendency toward auto-agglutination of the red cells because of a change in the electric charge. Hoeber and Mond [3] found that the negative charge of the red blood cells is greater in a solution of serum albumin, less in serum globulin and still less in fibrinogen. Dochez [4] and Krosing [5] showed that the fibrinogen content of the blood is usually increased in pneumonia, tuberculosis, peritonitis and other infectious diseases.

1. Fåhraeus, R.: Biochem. Ztschr. **89**:355, 1918.
2. Fåhraeus and Hoeber, quoted by Fischel.[14]
3. Hoeber and Mond: Klin. Wchnschr. **1**:2412, 1922.
4. Dochez, A. R.: J. Exper. Med. **16**:693, 1912.
5. Krosing: Arch. f. Gynäk. **93**:317, 1911.

These three findings probably combine to form the main factor causing an increased rate in many infectious diseases. That there are other factors is well known. Runnström and Schow [6] found an increased rate in animals following thyroidectomy, and it is a common clinical observation that persons with hypothyroidism have an increased rate while those with hyperthyroidism have an abnormally slow rate. Sachs [7] pointed out that epinephrine increases the rate of sedimentation, although Loehr [8] was of the opinion that it exerts no influence.

Bönniger and Hermann [9] pointed out that the number and size of the red blood cells exert an important influence, a theory supported by the fact that the sedimentation rate is decreased in polycythemia vera and in persons removing to high altitudes (Kapp [10]), while it is increased in severe anemia, although Greisheimer and his associates [11] found no constant parallel between the red blood cells and the rate of sedimentation. They likewise failed to correlate the rate of sedimentation with the weight, hemoglobin content and white blood cell count. In studies made to determine the relation of the sedimentation rate to fever the two were not found parallel. Starlinger [12] pointed out that the presence of colloidal particles in the blood may be an influencing factor, as may cholesterol. Leendertz [13] believed that antibodies may be an influencing factor.

This summary of the better known theories demonstrates that the causative factor or factors of a change in sedimentation rate are far from settled. They are treated more fully in an excellent article by Fischel.[14] It is my purpose to discuss still another factor, or perhaps the physiologic counterpart of one of those already mentioned, based on observations made at a children's sanatorium for tuberculosis.

OBSERVATIONS

The apparent sensitivity of the test in tuberculosis (Cutler and Cohen [15] believe it to be 94 per cent accurate in this disease) makes it excellent for routine procedure in a sanatorium for the treatment of patients with tuberculosis. For this reason the test has been used as a

6. Runnström, J., and Schow, S. A.: Acta Zool. **6**:131, 1920.
7. Sachs, H.: Kolloid-Beihefte **24**:113, 1919.
8. Loehr, quoted by Fischel.[14]
9. Bönniger, M., and Hermann, W.: Klin. Wchnschr. **2**:744, 1923.
10. Kapp, H.: Beitr. z. Klin. d. Tuberk. **68**:378, 1928.
11. Greisheimer, E. M., and others: Am. Rev. Tuberc. **16**:344, 1927.
12. Starlinger, quoted by Fischel.[10]
13. Leendertz, G.: Deutsches Arch. f. klin. Med. **137**:234, 1921.
14. Fischel, K.: Am. Rev. Tuberc. **10**:606, 1915.
15. Cutler and Cohen: Am. Rev. Tuberc. **21**:347, 1930.

routine on all new patients in the institution with which I am associated. As the result of this routine use my associates and I have made certain observations which we have not found discussed in the literature.

Early in the use of the test the rates reported in children were occasionally not commensurate with the clinical findings, but on repeating the test vastly different results were obtained without an intervening clinical incident to account for such a change. This observation has

TABLE 1.—*Cases in Which the Sedimentation Rate Decreased on Repetition of the Test*

Case	Age	Number of Days Between Tests	First Test, per Cent	Second Test, per Cent	Decrease, per Cent
L. R.	7	33	35	10	25
J. L.	6	14	50	32	18
W. D.	9	2	30	16	14
E. W.	6	10	40	26	14
D. M.	5	2	33	20	13
R. B.	5	23	56	45	11
S. N.	6	4	35	25	10
R. R.	6	11	31	22	8
A. K.	10	2	23	17	6
K. J.	9	2	18	12	6
A. K.	10	1	23	17	6
K. W.	11	2	12	7	5

TABLE 2.—*Cases in Which the Sedimentation Rate Increased on Repetition of the Test*

Case	Age	Number of Days Between Tests	First Test, per Cent	Second Test, per Cent	Increase, per Cent
L. T.	11	33	26	51	25
E. S.	5	11	42	66	24
E. P.	10	8	33	55	22
A. S.	11	33	25	46	21
E. C.	10	7	15	32	17
J. D.	13	8	35	49	14
L. G.	8	2	36	47	11
S. Z.	8	2	18	26	8
E. V.	7	1	6	13	7
A. K.	12	3	16	23	7
L. O.	14	1	30	37	7
T. O.	15	2	7	14	7
L. D.	7	2	16	22	6
H. Z.	10	2	26	31	5

been mentioned by two other writers, although the cause was apparently not considered by either. Spies [16] noted occasional exceptional values in children which he could not explain by errors in clinical findings, and Paradiso [17] noted that many infants in good general condition had greatly increased rates. In checking these unexplained high rates it was found that the second test gave a much lower rate, but in addition it was observed that many patients with a low rate on the first test showed a marked increase in the rate on the second test (tables 1 and 2).

16. Spies, F.: Beitr. z. Klin. d. Tuberk. **56**:67, 1923.
17. Paradiso, F.: Clin. pediat. **9**:723, 1927.

It was noted that many patients were unusually apprehensive and excited at the time of one of the tests, whereas at the time of the other they were not. Furthermore, the test taken at the time of the greater excitement gave the higher reading. The presence or absence of excitement was based purely on observation, and not on an index making it possible to measure the degree of excitement present. Attempts to measure its degree by pulse rates and blood pressure were not successful.

An attempt to explain this apparent discrepancy in the sedimentation rates calls to mind Cannon's observations on the increased activity of the suprarenal glands due to excitement. The theory that an outpouring of epinephrine might influence the sedimentation rate is supported by Sachs'[7] observations, but opposed by those of Loehr.[8] An attempt was made to check this possibility by adding a commercial brand of epinephrine to a specimen of blood, while a second specimen drawn at the same time from the same patient was allowed to go through sedimentation in the usual manner as a control. However, there was no great variance in the rates of sedimentation under these two conditions, although we satisfied ourselves that the presence of the preservative in the epinephrine which was used had no influence on the rate of sedimentation.

A possibility in the accurate checking of apprehension was suggested by Trumper and Cantarow,[18] who mentioned that: "Pain, emotional excitement, apprehension, fear, anger, etc., may raise the blood sugar above the resting level, probably through the medium of excessive secretion of epinephrine, resulting in increased hepatic glycogenolysis."

A preliminary attempt to check this observation was made by adding a solution of dextrose to blood in the process of sedimentation as epinephrine was added in the earlier experiment. This attempt was likewise not productive of results, though this observation is not conclusive, since it is probable that the dextrose of the blood stream is not identical with the dextrose known in chemistry.

The rates of sedimentation are being checked with the blood sugar content of specimens drawn at the same time, in order to establish a definite index of apprehension as indicated by Trumper and Cantarow. The results of this comparison are not yet complete, but give promise of showing a fairly consistently increased blood sugar content with increased sedimentation rates. The results of these observations will be reported when complete.

COMMENT

The observation that sedimentation rates in children show an unexplained tendency to vary widely without intervening clinical causes should be of value to pediatricians, regardless of the cause. That this

18. Trumper, M., and Cantarow, A.: Biochemistry in Internal Medicine, Philadelphia, W. B. Saunders Company, 1932, p. 22.

occurs commonly is demonstrated by the fact that 27 per cent of our patients had readings erroneous enough to mislead in their interpretation. Our experience, however, shows that a repeated test will usually give the correct reading. Occasionally a repeated test will show a persistently high rate, though this is not common. In such an event, careful clinical search should satisfy one as to the presence or absence of any condition warranting a high rate. A persistently high rate need serve, therefore, only as a warning of the possibility of the presence of a pathologic condition; it need not be held as conclusive.

Two sedimentation tests are done on successive days on all newly admitted patients, the lower rate being taken as the one reflecting the presence or absence of a destructive lesion. I am being forced to the conclusion that apprehension on the part of the patient is a factor in erroneous results in sedimentation tests, though I have not thus far been able to prove it. If such is the case, it will be necessary to repeat tests on patients giving a high rate as basal metabolic tests are now repeated. It is already well known that certain types of insanity are characterized by high rates of sedimentation and it is interesting to consider the possibility that the factor influencing the rate in this class of patients may be that of apprehension, because of emotional instability.

Later observations comparing blood sugar content with rates of sedimentation will be offered as a factor of proof or disproof of the contention that apprehension influences the rate of sedimentation.

THE BLOOD PROTEINS OF CHILDREN

II. DISTRIBUTION IN THE SAME SPECIMEN OF BLOOD OF HYDROLYZABLE, AMIDE, HUMIN, BASIC AMINO AND MONO-AMINO NITROGEN OF THE WHOLE BLOOD, RED CELLS AND SERUM PROTEINS

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The distribution of the total nitrogen in whole blood, red blood cells and serum proteins of the blood in children has been reported in a previous communication.[1] The present article records the results of further studies on the distribution of the amide, humin, hydrolyzable, basic amino and mono-amino nitrogen in the whole blood, red blood cells and serum proteins.

METHODS

The methods were adapted from those of Van Slyke [2] and Cavett.[3] The procedure for obtaining blood specimens, the separation of red blood cells and the serum proteins from the same specimen of blood and the determination of the total nitrogen have previously been described in detail.[1]

Whole Blood.—Five-tenths cubic centimeter of oxalated blood was diluted to 10 cc. with distilled water. One cubic centimeter was removed for the determination of the total nitrogen; the remaining 9 cc. was washed into a 30 cc. Erlenmeyer flask and 10 cc. of concentrated hydrochloric acid added. The flask, covered with a small funnel, was placed on a sand bath and heated for four hours, after which the flask was removed to a water bath and the contents evaporated to dryness, so as to remove all of the hydrochloric acid. Caution was exercised so that charring did not take place.

Red Cells.—The red cells obtained in the manner previously described [1] were dissolved in water and diluted to 10 cc. One cubic centimeter was removed for estimation of the total nitrogen. The remainder was hydrolyzed by the method described for whole blood.[4]

From the Achelis Laboratory and the A. Jacobi Division for Children, service of Dr. Jerome S. Leopold, Lenox Hill Hospital.

1. Bernhard, A.; Leopold, J. S., and Drekter, I. J.: The Blood Proteins of Children: I. Distribution of Total Nitrogen in Whole Blood, Red Blood Cells and Serum Proteins from the Same Specimen, Am. J. Dis. Child. **47**:1256 (June) 1934.

2. Van Slyke, D. D.: J. Biol. Chem. **10**:11, 1911.

3. Cavett, J. W.: J. Biol. Chem. **95**:335, 1932.

4. Bernhard, A., and Drekter, I. J.: Proc. Soc. Exper. Biol. & Med. **29**:1245, 1932.

Serum Proteins.—The serum proteins precipitated from 1 cc. of whole blood were dissolved in from 2 to 3 drops of a 10 per cent solution of sodium hydroxide, and water added to make 10 cc. One cubic centimeter was removed for determination of the total nitrogen and the remainder hydrolyzed as for whole blood.

Amide Nitrogen.—The contents of the flask after acid hydrolysis were diluted to 15 cc. with water and transferred to a heavy-walled, unlipped tube (6 by 1 inch, 50 cc. capacity) and 10 cc. of solution of magnesium hydroxide added (milk of magnesia, U. S. P., was found satisfactory for this purpose). Six drops of caprylic alcohol were added to prevent foaming. The mixture was aerated for one hour into 10 cc. of distilled water containing from 1 to 2 drops of a 10 per cent solution of hydrochloric acid, then nesslerized and diluted to suitable volume and compared in the colorimeter with a suitable standard nitrogen solution. The ammonia represented the amide nitrogen.

Humin Nitrogen.—The residue after the removal of the amide nitrogen was centrifugated and the supernatant fluid filtered into a 40 cc. graduated tube. The sediment was washed with from 3 to 5 cc. portions of water by centrifugation, the supernatant fluid filtered into a 40 cc. tube, and the final volume adjusted to 40 cc. The precipitate remaining in the tube was transferred to a Kjeldahl flask, to which 10 cc. of sulphuric acid was added, and the nitrogen determined in the usual manner. This represented humin nitrogen.

Total Nitrogen After Hydrolysis.—The filtrate from the humin nitrogen was diluted to 40 cc. Five cubic centimeters was removed for estimation of the total nitrogen. This represented the total nitrogen from hydrolysis after removal of the amide and humin nitrogen.

Basic Amino Nitrogen.—To the remaining filtrate 5 cc. of a 10 per cent solution of phosphotungstic acid in a 10 per cent solution of sulphuric acid was added, the contents mixed and allowed to stand in the refrigerator overnight. The mixture was then centrifugated and the precipitate washed with two 8 cc. portions of phosphotungstic acid. The precipitate was then dissolved in 2 cc. of a 10 per cent solution of sodium hydroxide and transferred to a 50 cc. volumetric flask. One drop of a 0.5 per cent alcoholic solution of phenolphthalein was added and neutralized with glacial acetic acid, after which the specimen was diluted to 50 cc. with distilled water (for the serum proteins the final dilution was 25 cc. instead of 50 cc.). Ten cubic centimeters was removed for determination of the total nitrogen. This nitrogen represented the total nitrogen of the basic amino nitrogen fraction precipitated by phosphotungstic acid. Throughout this article this fraction, which consisted of the arginine, lysine, histidine and one half of the cystine nitrogen, will be referred to as basic amino nitrogen.

Mono-Amino Nitrogen.—The filtrate remaining from the precipitation of basic amino nitrogen by phosphotungstic acid was neutralized with about 5 cc. of a 10 per cent solution of sodium hydroxide (when a slight precipitate formed, a drop of acetic acid dissolved it), and distilled water was added to make 50 cc. The total nitrogen was determined in 10 cc. of this solution when obtained from whole blood or from red cells, and in 20 cc. when obtained from serum proteins.

The mono-amino nitrogen was determined on 2 cc. portions by the Van Slyke [5] manometric method. This mono-amino nitrogen consisted chiefly of aspartic and glutamic acid nitrogen. The difference between the total nitrogen value of the filtrate and the mono-amino nitrogen represented the imino nitrogen, namely that in proline and oxyproline, and one half of the tryptophan nitrogen.

5. Van Slyke, D. D.: J. Biol. Chem. **16**:121, 1913.

It has been shown that repeated injections of aspartic acid produce hypertension in rabbits,[6] and that associated with this experimental hypertension there are definite changes in the basic amino nitrogen level of the serum proteins. Analogous changes in the serum protein values of human beings suffering from hypertension have also been recorded.[7] Since hypertension in children is uncommon, it was thought that a study of the blood proteins of children with reference to the basic and mono-amino nitrogen values of the serum proteins would be helpful in determining normal values for these fractions in persons with normal blood pressure.

The total, amide and humin nitrogen, total nitrogen after hydrolysis, basic amino and mono-amino nitrogen were determined in the whole blood, red cells and serum proteins from the same specimen of blood. This was done on forty-eight children whose ages varied between 5 months and 13 years and whose diets varied greatly. Neither age nor diet had an appreciable influence on the various nitrogen fractions.

NORMAL VALUES

Twenty-five children free from fever and cardiac, renal and metabolic disturbances and with normal blood pressure formed this group. The protein nitrogen constituents were determined as previously outlined, the high, low and average of the various fractions being shown in tables 1, 2 and 3. Normal values for adults are also included in the tables.

It is evident that the amide nitrogen values of whole blood, red cells and serum proteins do not show any significant variation from those found in normal adults. While the humin nitrogen was also determined in the majority of the specimens as a check on any undetermined nitrogen, the values are not reported because of the wide variations noted and because the humin nitrogen plays no rôle in the problem under consideration. The point of interest is the change in the basic amino and mono-amino nitrogen values, especially of the serum proteins. Since changes in the level of the basic amino nitrogen are usually compensated for by changes in the level of mono-amino nitrogen, we have introduced a ratio of the mono-amino nitrogen to the basic amino value which will be referred to as the M : B ratio.

Whole Blood.—In normal children the total nitrogen after hydrolysis varies between 2,740 and 1,410 mg. per hundred cubic centimeters, with an average of 2,078 mg. In adults the variation is between 3,180 and 2,460 mg., the average being 2,791 mg. It is evident that in normal

6. Rafsky, H. A.; Bernhard, A., and Rohdenburg, G. L.: Proc. Soc. Exper. Biol. & Med. **29**:1243, 1932.

7. Bernhard, A.; Leopold, J. S., and Drekter, I. J.: Proc. Soc. Exper. Biol. & Med. **29**:1248, 1932.

children the total nitrogen value of the whole blood after hydrolysis is lower than that of adults. The value for the basic amino nitrogen of the blood of normal children is about one-half that found in adults. Since the hemoglobin content of the blood of children is about 25 per cent lower than that of adults, one would expect to find the basic amino nitrogen level lower in the blood of children; the results obtained in these studies, however, are much lower than might be anticipated. The

TABLE 1.—*Nitrogen Distribution of the Whole Blood*

Case	Total Nitrogen	Amide Nitrogen	Total Nitrogen* After Hydrolysis	Basic Amino Nitrogen	Percentage of Total Nitrogen After Hydrolysis	Total Nitrogen of Phosphotungstic Acid Filtrate	Mono-Amino Nitrogen	Percentage of Total Nitrogen After Hydrolysis	M:B Ratio†
	Mg. per 100 Cc.					Mg. per 100 Cc.			
33151	2,710	107	2,120	600	28	1,580	1,480	70	2.5
21434	2,200	100	1,960	580	30	1,380	1,200	61	2.0
32693	2,820	127	1,410	455	30	970	960	70	2.2
33723	2,270	107	2,100	630	30	1,470	1,300	61	2.0
33447	2,760	107	2,520	490	19	2,020	1,990	79	4.0
34890	2,250	100	2,000	740	37	1,260	1,100	55	1.5
36104	2,200	100	1,940	570	29	1,380	930	48	1.6
33526	2,480	114	1,940	610	31	1,330	1,200	62	2.0
33570	2,130	100	1,970	530	27	1,430	1,200	60	2.3
32612	1,890	107	1,740	400	23	1,320	1,280	73	3.2
33264	2,560	127	2,160	450	21	1,720	1,720	79	3.8
33048	2,100	117	1,830	420	23	1,390	1,290	58	2.0
35117	2,490	113	2,070	450	22	1,620	1,540	74	3.4
33183	3,190	98	2,640	620	23	2,020	1,950	74	3.1
26866	2,550	108	2,020	460	23	1,520	1,400	70	3.0
33664	2,500	87	2,350	460	20	1,880	1,380	57	3.0
33721	2,810	147	2,540	600	23	1,930	1,440	56	2.4
32558	2,640	105	1,630	372	23	1,280	1,200	74	3.2
26287	2,360	...	2,130	570	26	1,590	1,180	55	2.0
34050	2,730	100	2,320	710	30	1,610	1,400	65	2.0
33116	2,680	100	1,930	520	27	1,430	1,300	68	2.5
32192	2,760	107	2,160	470	22	1,670	1,670	77	3.6
33468	2,520	107	2,100	510	24	1,600	1,600	76	3.1
36299	3,080	120	2,740	650	24	2,090	1,000	37	1.5
67970	2,060	82	1,620	422	26	1,200	1,100	68	2.6
High.....	3,190	147	2,740	740	37	2,090	1,990	79	4.0
Low.....	1,890	82	1,410	372	19	970	930	37	1.5
Average...	2,509	103	2,078	531	25	1,548	1,353	65	2.6
				Adults					
High.....	3,480	120	3,180	1,280	44	2,140	2,000	63	1.9
Low.....	2,700	100	2,460	890	31	1,400	1,200	48	1.1
Average...	3,035	109	2,791	1,056	37	1,715	1,515	54	1.4

* The total nitrogen value is determined after the removal of humin and amide nitrogen.
† M:B ratio means the ratio of the mono-amino nitrogen to the basic amino nitrogen.

percentage of this fraction of the total nitrogen after hydrolysis is slightly lower than that found in adults.

The mono-amino nitrogen value of the whole blood of children is also lower than that of adults. The values vary between 1,990 and 930 mg., with an average of 1,353 mg. per hundred cubic centimeters. In adults these respective figures are 2,000, 1,200 and 1,515 mg. In children the M:B ratio varies between 4 and 1.5, the average being 2.6, which is greater than that found in adults, in whom the ratio is rather constant, being between 1.9 and 1.1, with an average of 1.4.

Red Cells.—The amide nitrogen level of the red cells of the blood of children did not vary greatly from that of adults. The total nitrogen value of the red cells after hydrolysis was lower than that of adults. The high was 2,220, the low 930 and the average 1,523 mg. per hundred cubic centimeters, while for adults the variation was between 2,660 and 1,960, with an average of 2,231 mg. The difference between the levels

TABLE 2.—*Nitrogen Distribution of the Red Blood Cells*

Case	Total Nitrogen	Amide Nitrogen	Total Nitrogen* After Hydrolysis	Basic Amino Nitrogen	Percentage of Total Nitrogen After Hydrolysis	Total Nitrogen of Phospho-tungstic Acid Filtrate	Mono-Amino Nitrogen	Percentage of Total Nitrogen After Hydrolysis	M:B Ratio*
	Mg. per 100 Cc.					Mg. per 100 Cc.			
33151	2,030	87	1,680	440	26	1,240	1,200	70	2.7
21434	1,620	80	1,430	440	30	980	900	63	2.1
32693	1,850	70	930	322	34	630	630	67	2.0
33723	1,640	80	1,600	500	31	1,120	940	59	1.9
33447	2,140	87	2,020	360	18	1,650	1,650	82	4.7
34890	1,710	90	1,490	580	38	900	780	52	1.3
36104	1,500	80	1,270	420	33	850	530	41	1.3
33526	1,640	80	1,490	500	33	1,000	920	61	1.8
33570	1,500	77	1,430	400	28	1,020	970	68	2.4
32612	1,290	60	1,220	280	23	930	900	73	3.2
33264	1,820	87	1,620	330	20	1,300	1,300	80	4.0
33048	1,470	92	1,280	310	24	970	970	78	3.1
35117	1,790	70	1,580	320	21	1,270	1,200	76	3.7
33183	2,400	70	2,080	490	24	1,590	1,480	71	3.0
26866	1,830	70	1,540	348	23	1,200	1,100	71	3.1
33664	1,800	67	1,730	310	18	1,420	1,020	59	3.3
33721	2,150	100	2,040	480	23	1,550	1,100	54	2.3
32568	1,720	71	1,380	278	20	1,100	1,100	72	3.6
26287	1,710	..	1,520	450	30	1,070	850	56	1.9
34050	2,080	90	1,750	580	33	1,170	1,180	67	2.0
33116	2,000	80	1,380	380	28	990	980	71	2.6
32192	2,140	79	1,630	360	22	1,260	1,240	76	3.4
33468	1,680	70	1,510	390	26	1,110	1,100	73	2.8
36299	2,530	100	2,220	540	24	1,670	900	40	1.7
67970	1,460	60	1,250	280	22	900	850	68	3.0
High.....	2,530	100	2,220	580	38	1,670	1,650	80	4.7
Low.....	1,290	60	930	278	18	630	630	40	1.3
Average...	1,820	79	1,523	403	26	1,155	988	66	2.7
				Adults					
High.....	2,880	90	2,660	1,090	48	1,760	1,760	66	1.9
Low.....	2,100	80	1,960	730	31	1,030	900	40	0.9
Average...	2,430	89	2,231	895	40	1,342	1,220	54	1.3

* Footnotes to table 1 explain the values.

of the average total nitrogen of the whole blood after hydrolysis for children and adults was 713 mg., while for the red cells it was 708 mg.

The level of basic amino nitrogen of the red cells in children was 50 per cent lower than that of adults, owing in part to the lower hemoglobin content of the red cells in children. The mono-amino nitrogen value of the red cells in children averaged about 19 per cent lower than that in adults, whereas, the mono-amino nitrogen fraction of the total nitrogen level after hydrolysis averaged 12 per cent higher than in adults. The M:B ratio of the red blood cells was about twice as high as in adults.

Serum Protein.—The amide nitrogen value of the serum proteins of the blood in children averaged slightly higher than that in adults. The total nitrogen after hydrolysis of the serum proteins did not vary from that of adults. In children the basic amino nitrogen of the serum proteins varied between 160 and 100 mg., with an average of 125 mg. In only one instance was the basic amino nitrogen 100 mg., while in 88 per cent of the normal cases the variation was between 150 and

TABLE 3.—*Nitrogen Distribution of the Serum Proteins*

Case	Total Nitrogen	Amide Nitrogen	Total Nitrogen* After Hydrolysis	Basic Amino Nitrogen	Percentage of Total Nitrogen After Hydrolysis	Total Nitrogen of Phosphotungstic Acid Filtrate	Mono-Amino Nitrogen	Percentage of Total Nitrogen After Hydrolysis	M:B Ratio*
	Mg. per 100 Cc.					Mg. per 100 Cc.			
33151	690	20	500	160	32	340	280	56	1.7
21434	600	20	530	140	26	380	300	56	2.1
32693	800	57	480	126	26	360	360	75	2.8
33723	630	27	500	140	28	350	350	70	2.5
33447	640	20	500	130	26	370	370	74	2.8
34890	540	10	510	160	31	350	320	62	2.0
36104	680	10	660	150	22	510	400	60	2.6
33526	840	30	450	110	24	330	220	50	2.0
33570	610	23	530	130	24	400	230	43	1.7
32612	700	47	500	120	24	380	360	72	3.0
33264	750	40	540	120	22	420	420	77	3.5
33048	630	25	550	110	20	420	320	58	2.9
35117	700	40	520	120	24	380	330	66	2.7
33183	790	28	550	130	24	380	320	60	2.4
26866	710	30	520	110	21	420	380	72	3.4
33664	700	20	620	150	24	470	360	58	2.4
33721	660	47	500	120	24	380	340	68	2.8
32558	900	30	500	100	20	420	380	76	3.8
26287	630	..	610	120	20	490	320	52	2.6
34050	660	20	570	130	22	440	320	56	2.4
33116	680	20	540	120	22	420	330	61	2.7
32192	640	29	530	110	21	390	330	62	3.0
33468	840	37	580	120	21	460	460	80	3.8
36299	550	10	530	110	20	420	270	50	2.4
67970	590	22	470	140	29	330	280	60	2.0
High.....	900	57	660	160	32	510	460	77	3.8
Low.....	540	10	450	100	20	330	220	43	1.7
Average...	686	27	531	125	24	400	334	63	2.6
				Adults					
High.....	630	30	680	190	40	490	330	69	2.3
Low.....	530	10	450	120	23	280	190	38	1.0
Average...	591	19	543	159	29	379	274	50	1.8

* Footnotes to table 1 explain the values.

110 mg. In normal adults the basic amino nitrogen varied between 190 and 120 mg., the average being 159 mg. The percentage of the total nitrogen after hydrolysis expressed as basic amino nitrogen varied between 32 and 20, the average being 24. In adults this same percentage varied between 40 and 23, with an average of 29.

In children the mono-amino nitrogen value of the serum proteins was somewhat higher than that found in adults, the high for the normal group being 460 mg., the low 220 mg. and the average 334 mg. per hundred cubic centimeters, as compared with a high of 330 mg., a low of 190 mg. and an average of 274 mg. The percentage of this frac-

tion of the total nitrogen after hydrolysis varied between 77 and 43, with an average of 63, while in adults this same variation was between 69 and 38, the average being 50. The M : B ratio was higher in children than in adults, the variation in children being between 3.8 and 1.7, with an average of 2.6, while for adults it varied between 2.3 and 1, with an average of 1.8.

It is of more than passing interest to note that the average M : B ratio of the whole blood, red cells and serum proteins of children is

TABLE 4.—*Nitrogen Distribution of the Serum Proteins in Cases with Low Basic Amino Nitrogen Levels* *

Case	Age	Blood Pressure	Total Nitrogen* After Hydrolysis	Basic Amino Nitrogen	Percentage of Total Nitrogen After Hydrolysis	Total Nitrogen of Phosphotungstic Acid Filtrate	Monoamino Nitrogen	Percentage of Total Nitrogen After Hydrolysis	M:B Ratio*	Diagnosis
			Mg. per 100 Cc.			Mg. per 100 Cc.				
30092	4	136/84	510	60	12	450	480	92	8.0	1/9/32, acute nephritis; hypertension
		122/72	550	70	12	480	460	83	6.5	6/16/32
			550	60	11	500	500	90	8.3	10/10/32
		128/80	620	70	11	550	400	64	5.5	3/8/33
29543	7	108/84	520	60	11	460	420	81	7.0	3/11/32, acute tonsillitis; adolescent rickets
			480	60	12	420	400	83	6.6	4/25/32
			600	70	11	530	520	86	7.4	6/29/32
23151	12	124/66	480	80	17	390	340	71	4.5	Chorea endocarditis; acute fibrinous pericarditis
35246	11	132/52	640	100	15	540	530	82	5.3	Endocarditis with serofibrinous pericarditis
823	12	128/42	580	70	12	510	420	72	6.0	Chronic rheumatic fever; endocarditis
33673	4	.....	560	60	10	500	460	82	7.6	Chronic general lymphadenitis; incipient tuberculosis
16052	13	100/64	480	70	12	410	410	86	5.8	Sydenham's chorea
D3535	12	.....	480	95	20	400	300	63	3.1	Endocarditis and epilepsy
14158	6	84/60	590	70	12	520	440	74	6.3	Bronchopneumonia
33451	6	100/72	480	50	10	430	400	83	8.0	Lobar pneumonia

* Footnotes to table 1 explain the values.

rather constant, being, respectively, 2.6, — 2.7 and 2.6, while for adults the same ratios are 1.4, — 1.3 and 1.8.

OBSERVATIONS ON PATHOLOGIC CONDITIONS

It has been shown that the basic amino nitrogen of the serum proteins and its percentage of the total nitrogen after hydrolysis are fairly constant in normal children, the M : B ratio never being higher than 3.8. Changes in the basic amino nitrogen level and the M : B ratio occur in some pathologic conditions (table 4). Fifteen determinations

were made in ten cases, in two of which the examinations were made at intervals over a period of about one year. These two cases will be discussed in detail. The following diagnoses were made in the remaining eight cases: pneumonia (two cases), chorea and chorea with endocarditis, chronic rheumatic fever with endocarditis, chronic lymphadenitis with incipient tuberculosis, endocarditis and epilepsy and endocarditis with serofibrinous pericarditis.

In this group the basic amino nitrogen level of the serum proteins showed definite changes, varying between 100 and 50 mg., with an average of 69 mg. The percentage of the total nitrogen value after hydrolysis varied between 20 and 10, the average being 13. The lowest basic amino nitrogen value was found in a case of lobar pneumonia, in a patient of 6 years, with a blood pressure of 100 systolic and 72 diastolic. The highest occurred in a patient with endocarditis with serofibrinous pericarditis, aged 11 years, with a blood pressure of 132 systolic and 52 diastolic. The mono-amino nitrogen level varied between 530 and 300 mg., with an average of 432 mg., while the percentage of this fraction of the total nitrogen after hydrolysis was between 92 and 63, with an average of 79. The lowest figure was obtained in a case of endocarditis and epilepsy, while the highest occurred in a case of endocarditis with serofibrinous pericarditis, with normal urine and a blood pressure of 132 systolic and 52 diastolic.

The M : B ratio showed a marked increase over the normal, the variation for the eight cases being between 3.1 and 8. The one showing the highest ratio also had the lowest basic amino nitrogen level. In another instance, although the basic amino nitrogen level was the highest for the group with pathologic processes, the M : B ratio was also increased to 5.3.

Cases Studied Over an Extended Period.—CASE 30,092.—In a boy, aged 4 years, the condition was diagnosed as acute nephritis and hypertension. On Jan. 4, 1932, the blood pressure was 170 systolic and 120 diastolic, which fell by January 6 to 136 systolic and 84 diastolic. Determinations of the blood proteins made on January 9 showed the basic amino nitrogen value of the serum proteins to be low, 60 mg. (12 per cent of the total nitrogen after hydrolysis), and the mono-amino nitrogen to be 480 mg. (92 per cent of the total nitrogen after hydrolysis). The M : B ratio, 8, was high. The chemical examination of the blood for urea nitrogen and other constituents revealed normal conditions; the urine showed a faint trace of albumin and red blood cells, and in the urine concentration test the specific gravity varied between 1.022 and 1.005. The patient was discharged as improved. On June 16, 1932, the basic amino nitrogen of the serum proteins was 70 mg. (12 per cent of the total nitrogen after hydrolysis), the mono-amino nitrogen 460 mg. (83 per cent of the total nitrogen value after hydrolysis) and the M : B ratio 6.5. The blood pressure was 122 systolic and 72 diastolic. The blood pressure during July, August and September was, respectively, 122 systolic and 76 diastolic,

124 systolic and 72 diastolic and 128 systolic and 72 diastolic, values considerably higher than the normal averages for this age as reported by Richey.[8]

The blood proteins were again analyzed on October 10, at which time the basic amino nitrogen value was 60 mg. (11 per cent of the total nitrogen after hydrolysis), the mono-amino nitrogen 500 mg. (90 per cent of the total nitrogen after hydrolysis) and the M : B ratio 8.3, this being the highest ratio obtained in all our studies. Further examinations made on March 8, 1933, revealed the basic amino nitrogen value of the serum proteins as 70 mg. (11 per cent of the total nitrogen after hydrolysis), the mono-amino nitrogen 400 mg. (64 per cent of the total nitrogen after hydrolysis) and the M : B ratio, 5.5. The blood chemistry was normal, the phenolsulphonphthalein test showed 66 per cent elimination in two hours, and the blood pressure was 128 systolic and 80 diastolic. The outstanding points in this case were the persistent low basic amino nitrogen values, the increased mono-amino nitrogen values and the high M : B ratio.

Case 29,543.—A boy, aged 7 years, had a condition diagnosed as acute tonsillitis and adolescent rickets. The blood chemistry was normal. The urine had a specific gravity of 1.013 and contained a faint trace of albumin and hyaline and granular casts. The phenolsulphonphthalein test showed 37 per cent elimination in two hours. The blood pressure on March 11, 1932, was 108 systolic and 84 diastolic, and on March 28, 110 systolic and 84 diastolic. On March 11 the basic amino nitrogen value of the serum proteins was 60 mg. (12 per cent of the total nitrogen after hydrolysis), the mono-amino nitrogen 420 mg. (81 per cent of the total nitrogen after hydrolysis) and the M : B ratio 7. Determinations repeated on April 25 were essentially the same, except that the M : B ratio was 6.6. On June 29 the basic amino nitrogen value was slightly increased, being 70 mg. (11 per cent of the total nitrogen after hydrolysis), the mono-amino nitrogen 520 mg. (86 per cent of the total nitrogen after hydrolysis), and the M : B ratio 7.4.

On December 10 the child was readmitted to the hospital because of persistent vomiting of three months' duration, great weakness and failure to gain weight. No medication was given. The blood pressure on December 12 was 160 systolic and 120 diastolic; the nonprotein nitrogenous constituents of the blood were of normal value, and the urine was normal. The patient was considerably dehydrated, and intravenous injections of saline and dextrose solutions were given on December 13. The patient died. Postmortem examination revealed congestion and parenchymatous degeneration, with tubular degeneration and extensive necrosis of the kidneys. This case also showed a persistently low basic amino nitrogen value, an increased mono-amino nitrogen value and a high M : B ratio.

In abbreviated form we present the data in thirteen cases in which the basic amino nitrogen, the mono-amino nitrogen and the M : B ratio of the serum proteins were within normal limits.

Malnutrition.—Case 35,374.—In a child, aged 7 years, the blood pressure was 126 systolic and 68 diastolic; the urine was normal and the blood urea nitrogen level normal. The basic amino nitrogen value was 190 mg., the mono-amino nitrogen 400 mg. and the M : B ratio 2.1.

Case 19,878.—In a child, aged 7 years, the blood pressure was 90 systolic and 48 diastolic, the urine was normal and the blood urea nitrogen level normal. The basic amino nitrogen value was 140 mg., the mono-amino nitrogen 370 mg. and the M : B ratio 2.6.

8. Richey, H.: Blood Pressure in Boys and Girls Before and After Puberty, Am. J. Dis. Child. **42**:1281 (Dec.) 1931.

CASE 33,922.—In a child, aged 8 years, the blood pressure was 116 systolic and 84 diastolic; the urine was normal and the blood urea nitrogen level normal. The basic amino nitrogen value was 110 mg., the mono-amino nitrogen 200 mg. and the M : B ratio 1.8.

Acute Nephritis.—CASE 30,802.—In a child, aged 17 months, the blood pressure was 92 systolic and 66 diastolic. The blood showed a retention of nitrogen (urea nitrogen, 41.7 mg. per hundred cubic centimeters); the urine showed a faint trace of albumin, red cells and hyaline and granular casts, and there was a basic amino nitrogen value of 140 mg., a mono-amino nitrogen value of 400 mg. and a M : B ratio of 2.8.

CASE 33,609.—A child, aged 6 years, with acute nephritis, also had marked anemia, showing a hemoglobin concentration of 15 per cent, and a red blood cell count of 860,000. The blood pressure was 110 systolic and 80 diastolic, and the blood urea nitrogen level was 166, and the urine showed a trace of albumin, red cells and hyaline, granular and waxy casts. The basic amino nitrogen value was 110 mg., the mono-amino nitrogen 200 mg. and the M : B ratio 1.8.

CASE 33,908.—A child, aged 9 years, with acute and chronic nephritis and purpura haemorrhagica had a blood pressure of 124 systolic and 82 diastolic. The urine showed albumin, hyaline casts and red blood cells. The blood urea nitrogen level was normal. The basic amino nitrogen value was 120 mg., the mono-amino nitrogen, 380 mg. and the M : B ratio, 3.1.

CASE 26,747.—A child, aged 6 years, had a blood pressure of 110 systolic and 78 diastolic. The blood urea nitrogen was normal. The urine showed albumin, red blood cells and hyaline and granular casts. The basic amino nitrogen value was 160 mg., the mono-amino nitrogen 410 mg. and the M : B ratio 2.5.

Rheumatic Endocarditis.—In three children with rheumatic endocarditis, aged 5, 10 and 11 years, with blood pressures of 106 systolic and 60 diastolic, 122 systolic and 60 diastolic and 112 systolic and 58 diastolic, respectively, the basic amino nitrogen, mono-amino nitrogen and M : B ratio were normal.

Bronchopneumonia.—Two children, aged 16 months and 8 years, showed normal basic amino nitrogen and mono-amino nitrogen concentrations. The M : B ratio was 2 and 3. One child, aged 10 years, suffering from pyelitis, obesity and hypertension, with a blood pressure of 132 systolic and 90 diastolic, a normal blood urea nitrogen and urine containing albumin and pus cells, showed normal basic amino nitrogen and mono-amino nitrogen concentrations and M : B ratio.

CONCLUSIONS

1. A procedure is described for the determination of amide, humin, hydrolyzable, basic amino and mono-amino nitrogen of the whole blood, red cells and serum proteins from the same specimen of blood.

2. In normal children the amide nitrogen of the whole blood, red cells and serum proteins did not show significant variations from that found in normal adults.

3. The values for total nitrogen after hydrolysis, basic amino nitrogen and mono-amino nitrogen in normal children are lower than those in adults. The M : B ratio is higher than that of adults.

4. In normal children the values for hydrolyzable, basic amino and mono-amino nitrogen of the red cells of the blood are lower than those in adults. The M : B ratio of the red cells is higher than in adults.

5. The basic amino nitrogen value of the serum proteins of children is lower than that of adults, while the mono-amino nitrogen level is higher. The M : B ratio of children is higher than that of adults.

6. In ten cases of pathologic conditions the basic amino nitrogen was decreased and the mono-amino nitrogen increased, and there was a sharp rise in the M : B ratio. In two cases of hypertension the basic amino nitrogen value was low, while the mono-amino nitrogen and the M : B ratio were increased.

Case Reports

VASCULAR OCCLUSION IN PNEUMONIA

REVIEW OF THE LITERATURE AND REPORT OF A CASE

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The complications of pneumonia are many, varied and usually not fatal. Among the least common are occlusion of the blood vessels due to embolism and thrombosis. Although these lesions have been recognized for many years, comparatively few persons have had the opportunity to observe them. The arteries or the veins may be involved, the veins more commonly than the arteries. Steiner,[1] in 1902, reported fifty-four cases selected from the literature in which there was venous involvement complicating pneumonia.

We propose to deal only with arterial occlusions and the resulting lesions. In reviewing the literature we have selected for analysis thirty-one cases, and have added the report of a case which was recently observed at the Children's Memorial Hospital. A number of other cases of vascular lesions developing in pneumonia have been reported in the literature, but after careful analysis we have excluded them from the present series for reasons to be given later. We recognize, however, that in these cases the pneumonia was an exciting factor.

Arterial occlusion is uncommon in pneumonia, and the reported cases have been widely separated in years. The first authentic record that we have found of arterial embolism or thrombosis complicating pneumonia was that of a case observed by Reddy,[2] in 1879.

His patient was a man, aged 27, who had lobar pneumonia on the right side which later migrated from one lobe to another. The crisis occurred on the ninth

From the Department of Pathology and Pediatrics of the Children's Memorial Hospital.

1. Steiner, W. R.: Peripheral Venous Thrombosis in Pneumonia, Johns Hopkins Hosp. Rep. **15**:189, 1902.

2. Reddy, J.: Pneumonia of the Right Lung Followed by Embolism of the Right Femoral Artery with Gangrene, Amputation of the Thigh and Recovery, Canad. M. & S. J. **8**:151, 1879.

day, and on the same day he had sudden and severe symptoms of arterial occlusion of the right lower extremity. The occlusion was complete, and gangrene followed. The gangrenous member was later amputated and the patient recovered.

Sir William Osler [3] saw only one case in a long and active practice. Howard,[4] in his monograph on the diagnosis and treatment of pneumonia, mentioned that such lesions occur, but said that he had never observed one. There is not a record of a case in either the Children's Memorial Hospital or the Montreal General Hospital, the latter over a hundred years old.

ANALYSIS OF CASES

The following critical analysis of thirty-two cases showing arterial occlusion during pneumonia will give some idea of the course and type of pneumonia in which arterial occlusion occurs and the result of the pneumonia and of the occlusion.

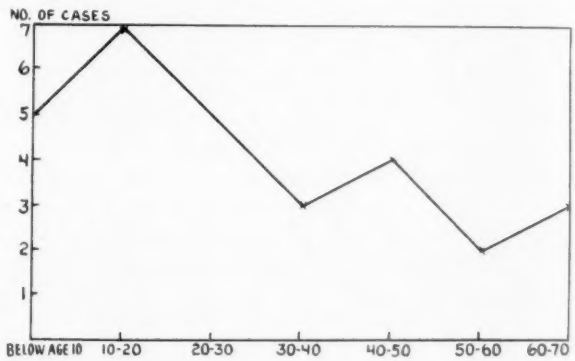

Fig. 1.—Age of patients reported in the literature in whom arterial occlusion developed complicating pneumonia.

Age and Sex Incidence.—Age probably plays little part, since occlusions occurred in persons from 15 months to 67 years of age. The majority occurred during the first thirty years of life. This would be expected, since embolism and thrombosis commonly follow lobar pneumonia, and lobar pneumonia is more often seen during this period. The average age was 29 years; thirteen patients were under 20 years, five from 20 to 30, three from 30 to 40, four from 40 to 50, two from 50 to 60 and three from 60 to 70. In four reports the age was not mentioned (fig. 1). Males were more frequently affected than females, the proportion being two to one.

3. Osler, W., and McCrae, T.: Principles and Practice of Medicine, ed. 3, Philadelphia, Lea & Febiger, 1925, vol. 4, p. 895.

4. Howard, C. P.: Diagnosis and Treatment of Pneumonia, Oxford Monograph, New York, Oxford University Press, 1931, vol. 10, p. 147.

Relation of Vascular Occlusion to Pneumonia.—The condition occurred more frequently in lobar pneumonia. Twenty-three had lobar pneumonia, five bronchopneumonia, and in four the type was not stated. The upper lobe of the right lung was involved in two, the middle lobe of the right lung in one, the lower lobe of the right lung in thirteen, the upper lobe of the left lung in one, the lower lobe of the left lung in four, and in two cases the involved lobe was not stated. In two cases there was pneumonia of the migratory type.[5]

The symptoms at onset and the course of the pneumonia seemed to have little bearing on the occurrence of vascular occlusion. The mild and severe cases were about equally distributed. In twelve the temperature fell by crisis on the fourth to the twelfth day, the average being the eighth day. In four the temperature fell by lysis and in sixteen the type of termination was not given. Arterial embolism and thrombosis in pneumonia occur most frequently soon after the temperature has reached normal. In two cases it occurred on the day of the crisis,[6] and in one [7] it occurred twenty-nine days after the onset of symptoms of illness. The latter was a case of bronchial pneumonia which ran a mild course, with the temperature falling by lysis.

During the period of convalescence, symptoms and signs of arterial occlusion were noted. Superficial gangrene of the toes appeared. Collateral circulation was adequate and recovery followed. In the remaining twenty-nine cases the arterial lesions occurred at various periods of the illness, the average being the eleventh day after the onset of pneumonia.

Symptoms.—In the majority of cases the symptoms of arterial occlusion were sudden and severe. The first symptom in most cases was pain followed by hyperesthesia, numbness and tingling, loss of sensation, local pallor and blotchy cyanosis, followed either by gangrene or by the establishment of collateral circulation and partial or complete recovery.

Location of the Occluded Artery.—In the thirty-two cases the occlusion occurred in the following: The left lower extremity, five

5. (*a*) Fette, H.: Ueber arterielle Thrombose in Verlauf der kruppösen pneumonia, Med. Klin. **5**:734, 1909. (*b*) Reddy.[2]

6. (*a*) Brourardel, M. G., and Giroux, M. R.: Artérite aigue de l'humérale postpneumonique; évolution sans gangrène, Bull. et mém. Soc. méd. d. hôp. de Paris **35**:1268, 1913. (*b*) Gibson, C. L.: Embolic Gangrene of the Leg as a Sequel of Acute Lobar Pneumonia, Ann. Surg. **38**:380, 1903.

7. Head, George: Acute Arteritis Complicating Pneumonia, Am. J. M. Sc. **162**:157 (Aug.) 1921.

(four from the literature[8] and our case); the right lower extremity, six;[9] both lower extremities, four;[10] bilateral, superficial gangrene of the toes, one;[11] the right foot, with superficial gangrenous patches over the right knee, elbow and shoulder, one;[12] the right upper extremity, one;[6a] the left upper extremity, two;[13] both upper extremities, one;[14] the fingers of the right hand, one;[15] one upper and one lower extremity, one;[16] an extremity, location not given, three;[17] the cerebellar artery with gangrene and meningitis, one;[18] the right sylvian

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8. (*a*) Berthier, André: Contribution à l'étude de la gangrène des extrémités dans la pneumonie, Thèse de Paris, 1899. (*b*) Heiman, H.: A Study of Pneumonia in Infancy and Childhood During Recent Epidemics, Am. J. Dis. Child. **20**:119 (Aug.) 1920. (*c*) Wise, W. D., and Mayer, E. E.: Gangrene of an Extremity as a Complication of Pneumonia, Ann. Surg. **74**:565, 1921. (*d*) Gibson.[6b]

9. (*a*) Ardin-Delteil; Lévi-Valensi, and de Peretti: Un cas de gangrène du gros orteil ayant fait suite à un pneumonie; traitement par le citrate de soude; guérison, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1107, 1924. (*b*) Hamilton, F. H.: Embolism of the Femoral Artery Following Acute Lobar Pneumonia, New York M. J. **32**:63, 1880. (*c*) Irish, R. H.: Report of a Case of Embolism of the Popliteal Artery Following Pneumonia, Albany M. Ann. **23**:205, 1902. (*d*) Woodman, W. B.: Broncho-Pneumonia with Gangrene, M. Times & Hosp. Gaz., London **2**:329, 1863. (*e*) Reddy.[2] (*f*) Gibson.[6b]

10. Attix, F. F.: Double Embolic Gangrene of the Lower Extremities as a Complication of Pneumonia, J. A. M. A. **46**:1287 (April 28) 1906. Lee, H. J.: Report of a Case of Gangrene of Both Legs Following Pneumonia, Cleveland M. J. **6**:225, 1907. Perrier, H.: Gangrene of Heels in Infants with Bronchial Pneumonia, Rev. méd. de la Suisse Rom. **45**:300 (April) 1925. Thomas, C. P.: Double Popliteal Embolism Complicating Pneumonia, Am. J. Surg. & Gynec. **16**:198, 1902.

11. Head, G.: Am. J. M. Sc. **162**:157 (Aug.) 1921.

12. Zuppinger: Die Spontangangrän im Kindesalter, Wien. klin. Wchnschr. **12**:335, 1899.

13. Thurber, L.: Pneumonie des lobes moyen et inférieur droits: Suppression des pouls de la radiale et de la cubitale gauches, Rev. méd. de la Suisse Rom. **7**:44, 1887. Munk, J.: Gangrène spontanée, Arch. de méd. d. enf. **1**:437, 1898.

14. Fussell, M. H.: Certain Complications of Pneumonia, Am. J. M. Sc. **137**:67, 1909.

15. McGregor, A. N.: Gangrene of the Extremities After Pneumonia with Notes of Two Illustrative Cases, Glasgow M. J. **70**:81 (Aug.) 1908.

16. Kiefer, E. D.; Brigham, F. G., and Wheeler, R. R.: Embolic Gangrene of the Extremities in Pneumonia: Report of a Case Occurring in Diabetic Coma with Sugar Content of Cerebrospinal Fluid During Insulin Shock, Boston M. & S. J. **194**:191 (Feb. 4) 1926.

17. Fette.[5] Head.[7] Gibson.[6b]

18. Deshmukh, P. L.: Two Cases of Pneumonia with Thrombosis in Brain, Having Bearing on Pathogenesis of Remote Pneumococcal Complications in Pneumonia, Indian M. Gaz. **65**:446 (Aug.) 1930.

artery, one;[19] hemiplegia and the left upper extremity, one;[20] left hemiplegia, one;[20] the lenticulo-optic artery, one;[21] and the basilar artery, one.[22]

From the foregoing list it will be seen that the extremities were most commonly involved, in twenty-seven of the thirty-two cases. In seventeen the lower extremities were involved, and in sixteen there was unilateral and in seven bilateral involvement. Of the cases with unilateral involvement, in five the occlusion was on the same side as the pneumonia, in three it was on the opposite side and in three the site of the pneumonia or the site of the vascular lesion was not given. In ten of the sixteen cases of unilateral involvement, the pneumonia was lobar, in three it was bronchial, and in three the type was not mentioned.

Mortality.—Eleven patients died from the sixth to the thirty-first day after embolism or thrombosis occurred. Only two had an extremity amputated. The ages of the patients who died were 1½, 18, 19, 27, 29, 32, 41, 56 and 61 years, and the age was omitted in one report. The average age was 30 years. Death occurred in four cases in which arteries of the brain were occluded, in three in which arteries of two extremities were occluded and in four in which a single extremity was involved.

Recovery.—In fifteen of the remaining twenty-one cases gangrene developed, which did not clear as a result of canalization or collateral circulation, and amputation was done. In five of the remaining six recovery followed the establishment of collateral circulation, and in one [20] the result was not given. In one of the five cases with recovery [6a] the right humeral artery was occluded, and collateral circulation was adequate. In another [11] there was only superficial gangrene of the toes, and collateral circulation was adequate. In another,[20] hemiplegia gradually cleared, and in another [9a] an artery of the foot was occluded, and collateral circulation was adequate.

ETIOLOGY

Arterial lesions may be due to an embolus or to actual arteritis with thrombus formation. We are unable to give the incidence of these two lesions. Various theories have been advanced to explain arterial lesions.

19. de Massary, F., and Boquien, Y.: Multiple Cerebral Thromboses as Complication of Pneumonia, Bull. et mém. Soc. méd. d. hôp. de Paris **53**:1100 (July 22) 1928.

20. Favre, A.: Pneumonie du sommet droit hémiplégie gauche; suppression du pouls de la radiale droit, Rev. méd. de la Suisse Rom. **6**:285, 1886.

21. Aldrich, C. J.: A Case of Embolism of One of the Right Lenticulo-Optic Arteries, Complicating Pneumonia, M. News **74**:124, 1901.

22. Suckling, R.: Right Hemiplegia from Cerebral Thrombosis Complicating Pneumonia, Birmingham M. Rev. **30**:94, 1891.

Keen [23] said: "Emboli are usually of cardiac origin, although they may come from thrombi which have formed in the vessels between the heart and the extremities." McCrae [3] said: "It is due to an enfeebled circulation." Howard,[4] Gibson [6b] and Wise and Mayer [8c] believe that the lesions were caused by emboli arising from thrombi in the pulmonary veins in the pneumonic lung or from cardiac thrombi. Patients in whom endocarditis develops during pneumonia usually die, while patients in whom thrombi and emboli complicate pneumonia usually recover. This would indicate that arterial occlusion due to embolus or thrombus in pneumonia has as its origin some other area than the heart. Albutt and Rolleston [24] and Head [7] believed that thrombosis was caused by pneumococci in the blood stream resulting in arteritis.

We found that the symptoms of arterial occlusion in most cases were sudden and severe, suggesting embolism rather than thrombosis.

In addition to the thirty-two cases of arterial occlusion, there are twenty-five others reported as cases of arterial embolism or thrombosis complicating pneumonia. We have not included these in our series because there were other accompanying lesions which are more prone to cause thrombosis or embolism than is pneumonia. We realize, however, that pneumonia was an exciting factor.

Among these twenty-five cases were eleven in which there was either clinical or pathologic evidence of heart disease.[25] In three cases [26] the

23. Keen, W. W.: Surgery: Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1916, vol. 1, p. 45.

24. Albutt, T. C., and Rolleston, H. D.: A System of Medicine, New York, The Macmillan Company, 1909.

25. (*a*) Benedikt, W.: Gangrän des Fusses als Complication einer croupösen Pneumonia, Wien. med. Presse **32**:1206, 1891. (*b*) Malherbe: J. méd. sect. de Soc. acad. Loire infer. **19**:121 and 205, 1843. (*c*) Rendu: Thrombose de l'artère illias et de artère rénale au cours d'une pneumonie infectieuse; gangrène massive des deux membres inférieurs, Bull. et mém. Soc. méd. d. hôp. de Paris **3**:19 (Jan. 15) 1892. (*d*) Hervey, R.: Embolie de l'artère fémorale et gauche survenue chez un sujet atteint de pneumonie et d'athrome de la partie supérieure de l'orte, Bull. Soc. anat. de Paris **48**:216, 1873. (*e*) Hoepffner, C.: Ein Fall von Embolie in die Arteria radialis und ulnaris des linken Armes, München. med. Wchnschr. **56**:183 (Jan. 26) 1909. (*f*) Kredel, L.: Embolische Extremitätengangrän noch Pneumonie, Deutsche Med.-Ztg. **25**:1024, 1904. (*g*) Price, J.: Case of Senile Gangrene Following Pneumonia, Cincinnati Lancet **8**:688, 1860. (*h*) von Grimm, A.: Ein Fall von Gangrän der Hand noch doppelseitiger Pneumonie, New Yorker med. Monatschr. **4**:288, 1892. (*i*) Walsh, N.: Unusual Complications of Pneumonia, Brit. M. J. **1**:394 (March 10) 1928. (*j*) Dévé and Mompeurt: Infarctus du cours par thrombo-artérite pneumonique, Rev. méd. de Normandie **10**:237 (July) 1909. (*k*) Luc: Gangrene momifiante du pieds gauche, Bull. de la Soc. Anat., 1888.

26. Reilly, E. A.: Pneumonia, Gangrene, New York M. J. **59**:685, 1894. Barraud, S.: Ueber Extremitätengangrän in jugendlichen Alter nach Infectionskrankheiten, Deutsche Ztschr. f. Chir. **74**:237, 1904. Seidelman, W.: Ein Fall von symetrischer Gangrän der extremitäten nach Pneumonie, Deutsche Ztschr. f. Nervenh. **27**:114, 1904.

condition was diagnosed as Raynaud's disease. In two,[27] the patients were Negroes, 23 and 31 years of age, respectively, who had a history of syphilis and positive Wassermann reactions of the blood. Two patients [28] were old people, 60 and 92 years of age, with advanced arterial sclerosis. One patient [29] had pneumonia from which he recovered completely. Two months later, while working, he was seized with symptoms of bilateral arterial occlusion of the lower extremities. A short time later he died. At postmortem examination clots were found in the middle cerebral artery on the right side and hemorrhagic infarcts in the upper portion of the right lung. In one case [30] the occlusion occurred three years following apparent complete recovery from pneumonia. In four cases [31] the lesions were considered to be venous. One case [32] was that of a patient with malaria in whom pneumonia developed and, later, an area of gangrene on one cheek.

REPORT OF A CASE

History.—A girl, aged 5 years, was admitted to the Children's Memorial Hospital, service of Dr. S. J. Usher, on Sept. 15, 1932. She was perfectly well until September 11, when she fainted while getting out of bed—the first time such a thing had ever happened. During the day fever, diarrhea, anorexia and vague abdominal pain appeared. Two days later she had improved sufficiently to return to school.

On September 14, three days after the onset of the illness, she felt feverish again and vomited five times, always small amounts and of fluid consistency. The abdominal pain was more severe now than during the first attack and had become generalized. On the afternoon of September 14 her breathing became rapid.

On September 15, four days after the onset of the illness, she had three convulsions, each lasting about five minutes. During these her eyes rolled from side to side, and there were fine twitching movements of the face and hands. A few minutes of sleep followed each convulsion.

The patient had pneumonia two years prior to admission, at which time she was confined to bed for five weeks. There was complete recovery. There was no history of other illness. She had been vaccinated against smallpox ten days before admission. The mother, father and three other children were alive and well.

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27. Bailey, S. P.: Gangrene of the Extremities Complicating Pneumonia, J. Tennessee M. A. **16**:89, 1923. Head.[7]

28. Blagdon, J. J.: A Case of Thrombosis of the Femoral Artery Following Pneumonia, St. Barth. Hosp. J. **5**:122, 1897-1898. Deshmukh.[18]

29. Pye; Smith, and Porter: Pneumonia, Convalescence, Gangrene of Both Feet, Lancet **2**:1143, 1884.

30. Crisp: Med.-Chir. Tr. London **24**:451, 1836.

31. Croker, P. A., and Newman, F. J.: Pleuropneumonia, Empyema-Thrombosis of the Thigh, Australian M. J. **4**:267, 1883. Mori, A.: Gangrene of the Lower Extremities Caused by Pneumonia, Gazz. d. osp. **21**:725, 1900. Woodman.[9d] Hoepffner.[25e]

32. Hull, G. S.: Gangrene of the Cheek Following Pneumonia, Univ. M. Mag. **3**:27 (Oct.) 1890.

Examination.—The child looked toxic, was lethargic and showed marked dyspnea and cyanosis. The mark of recent vaccination was seen on the arm. The pulse was regular in rate (134 per minute) and rhythm, though the volume was small. Percussion revealed no enlargement. The heart sounds were well heard and normal. There was slight generalized tenderness in the upper portion of the abdomen on deep palpation, but no localized tenderness. No masses were felt.

Neurologically there were no positive findings except restlessness.

Respiration was mostly abdominal. There were dyspnea and cyanosis, but no cough or herpes. Percussion revealed slight impairment along the vertebral border of the left scapula. The breath sounds were slightly harsher on the left than on the right, but no râles or friction rub was heard.

On admission the temperature was 102 F.; the red blood cell count, 3,470,000; the white blood cell count, 12,000, of which 80 per cent were polymorphonuclear leukocytes, and the hemoglobin content, 65 per cent (Sahli). The urine was normal.

The diagnosis was early bronchopneumonia.

Course.—On September 15 roentgenograms of the chest showed a slight haziness and some mottling of the fields of both lungs, suggestive of bronchopneumonia. On September 17 the temperature was 100.5 F., the pulse rate, 150 and the volume good. The breath sounds in the left axilla were harsh, and fine moist râles could be heard over this area. On September 18 the pulse rate was 140 and the temperature from 99 to 100 F.; the cyanosis had decreased somewhat. Up to that time the progress of the case was that commonly seen in bronchopneumonia in childhood.

On September 19, at 1:30 p. m., the child complained of sudden cramplike pain in the sole of the left foot. This member was blanched, and the great toe was held in plantar flexion. The pain was thought to be due to muscular spasm, so heat was applied. The temperature was 100.5 F. and the pulse rate 130. At 8:30 p. m. the pain in the foot remained the same, and there was some pain in the calf of the left leg.

On September 20 there was extreme pain in the left knee and lower part of the left leg and foot. The left leg was much colder than the right from the knee down. The left foot was blanched, and there were scattered areas of cyanosis. There was no pulsation in the left dorsalis pedis or in the posterior tibial or popliteal arteries. Thermal tests of both legs and feet were made by means of a thermopile before and after the administration of spinal anesthesia (fig. 2). The left leg during the preliminary test was much colder than the right. After the administration of spinal anesthesia there was no increase in the temperature in the lower portion of the left leg. From these tests and other clinical findings a diagnosis was made of arterial occlusion at about the level of the bifurcation of the popliteal artery.

On September 21 the temperature was 100 F. and the pulse rate, 140. There was definite gangrene in the left foot.

On September 22 the following note was made (Dr. W. W. Eakin, cardiologist): "The temperature is 103 F., the pulse rate, 140 per minute and regular, and the blood pressure, 102 systolic and 70 diastolic. The heart is displaced a little to the left, and there is slight enlargement. The sounds are regular and well heard in all areas, and there are no murmurs. There are no findings in the heart suggesting a lesion from which an embolus could have arisen." An electrocardiogram showed all the leads normal.

On September 26 the temperature varied between 101 and 103 F., and the pulse rate was 120. The gangrene appeared to be stationary, and there was now a definite line of demarcation.

On September 27 the patient's general condition was improving. The line of demarcation on the lower part of the leg was sharp and stationary. The patient continued to improve and the line of demarcation of the gangrene remained stationary.

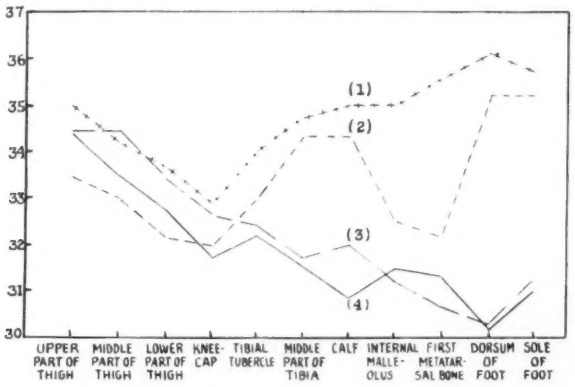

Fig. 2.—The skin temperatures of the lower extremities before and after the administration of spinal anesthesia: *1*, temperature of the right leg after spinal anesthesia; *2*, temperature of the right leg before spinal anesthesia; *3*, temperature of the left leg after spinal anesthesia, and *4*, temperature of the left leg before spinal anesthesia. The affected leg failed to show vasodilatation after spinal anesthesia had been administered.

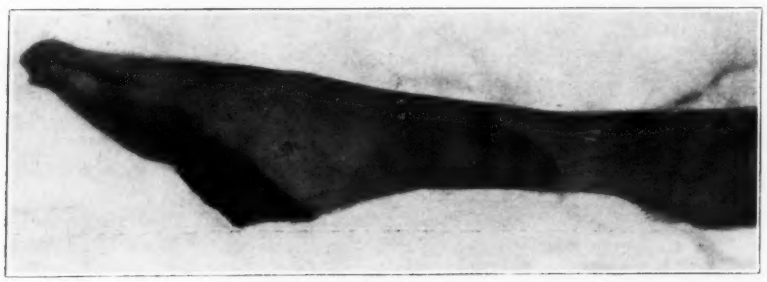

Fig. 3.—The gangrenous leg just before amputation.

On October 4 the temperature remained about 100 F., and the pulse rate was from 100 to 110. Amputation under spinal anesthesia was decided on and was begun at the middle of the lower part of the leg. Pus was encountered beneath the fascia, so the operation was discontinued. During the following fourteen days the patient's general condition improved; the signs and symptoms of pneumonia disappeared, the gangrenous area remained stationary and the pus disappeared.

On October 18, under spinal anesthesia, the left leg was amputated by Dr. R. R. Fitzgerald, attending surgeon, 4 inches (10.16 cm.) below the spine of the tibia. The hooded flap method was used.

On October 28 roentgenograms showed much improvement in the pneumonic condition. The temperature was normal and the pulse rate was 110.

On November 4 the patient was discharged from the hospital in good condition. The operative wound was completely healed.

The patient was seen by us in the outpatient department on two occasions, one and two months after discharge from the hospital. The chest was normal, both clinically and by roentgen examination. There were no heart murmurs and no cardiac enlargement. The site of the amputation was well healed.

Pathologic Report on the Amputated Leg.—The specimen consisted of the left foot and the lower two thirds of the left leg. Dry gangrene of the entire foot and ankle was well demarcated about 1½ inches (3.7 cm.) below the level of amputation. The toes were dry and had begun to shrivel. The amputation was done at a level which showed viable tissue. The arteries and veins were dissected from the amputation level down to their termination in the small vessels of the foot and no thrombus was found. The arterial occlusion must have been above the level of amputation.

The diagnosis was gangrene of the lower part of the left leg and left foot.

INFLUENZAL MENINGITIS AND PERITONITIS

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Influenzal meningitis is comparatively frequent in children. Influenzal peritonitis either has occurred infrequently or been little stressed. Isnardi [1] reported a case in 1892. Hill [2] and Fisch [3] reported the first case in America in 1903. Davis [4] and Rivers [5] later mentioned the condition but paid it little heed. The fact that some organisms change their site of insult as years pass warrants emphasis on this condition.

Influenzal meningitis occurs in early life. Davis [6] reported the youngest patient. The child, a twin, was taken sick on the fifth day of life and died on the ninth. The organisms were recovered at autopsy. The other twin was taken sick at the same time and died on the twelfth day, but neither spinal puncture nor autopsy was performed.

REPORT OF A CASE

History.—The patient, B. F., a white female infant, born following a normal hospital delivery, was transferred to the pediatric service of Dr. Hugh Kennedy, Hillman Hospital, Birmingham, Ala., with the complaint of high fever (104 F.). An infant born of the same mother two years previously became ill on the fifth day of life and died on the fourteenth. The physician diagnosed the condition meningitis, but failed to ascertain the type. Other members of the family had always enjoyed good health.

Course.—The child became sick on the fourth day of life. The following day it refused to nurse, and its skin became dry and hot. One day later meningeal involvement was suspected. Spinal puncture revealed a cloudy fluid under pressure which on microscopic examination and culture disclosed Bacillus influenzae. The following day, twitching, unilateral blanching and bulging of the fontanel were noted. The skin later became cyanotic and breathing labored. There was an increase of leukocytes to 24,350 and of polymorphonuclears to 89 per cent. The child died on the nineteenth day of the illness.

Contribution 36 from the Department of Biology and Public Health, Massachusetts Institute of Technology.

1. Isnardi, L.: Peritonite da influenza, Gior. d. r. Accad. di med. di Torino **40**:284, 1892.
2. Hill, Roland: A Case of Grip Peritonitis, St. Louis M. Rev. **47**:19, 1903.
3. Fisch, Carl: Pathological Findings in a Case of Grip Peritonitis, St. Louis M. Rev. **47**:55, 1903.
4. Davis, D. J.: Influenzal Meningitis with Especial Reference to Its Pathology and Bacteriology, Am. J. Dis. Child. **1**:95 (April) 1911.
5. Rivers, T. M.: Influenzal Meningitis, Am. J. Dis. Child. **24**:102 (Aug.) 1922.
6. Davis, D. J.: Influenzal Meningitis, Arch. Int. Med. **4**:323 (Oct.) 1909.

Necropsy.—Examination revealed a white baby girl, 21 inches long, weighing 6.5 pounds (2,948 Gm.). Small petechiae were present on the face and red blotches over the entire body. Yellowish, glistening, friable and flakelike patches were noted on the surface of the liver, spleen, portions of the parietal peritoneum, mesentery and intestines. On the upper portion of the ileum were many petechiae and an area about 6 inches (15 cm.) long which appeared hemorrhagic. The mesenteric lymph nodes were enlarged. The plaques were easily scraped off, being bound down by a fine fibrin. Beneath them were small petechiae. The plaques yielded B. influenzae. The first transplant of the organism grew well on agar. There is no doubt that the X and V factor necessary for its growth was carried to the medium in the transplant. The organism was predominantly long and threadlike, as is characteristic in influenzal meningitis. There was no fluid in the abdominal cavity. The remainder of the organs showed acute inflammatory lesions. On opening the dura, there was a gush of cloudy fluid containing a flaky material similar to that seen in the abdomen. On the surface of the brain, especially in the region of the blood vessels and at its base, were plaques of a fibrinous nature similar to those found in the abdomen. The vessels of the brain were extremely congested. There were pronounced disintegration and necrosis in the region of the cerebellum. On section, the brain showed extreme edema and congestion. The ventricles and choroid plexus appeared to be eaten away by an extremely malignant type of necrosis. An organism similar to the one already described was recognized in microscopc sections of the involved areas after using Mallory's stain for B. influenzae.

COMMENT

This case illustrates the extensiveness of influenzal involvement in an infected infant. Malignant necrosis, edema and small hemorrhages were characteristic of the brain lesions. The peritoneal involvement, however, showed comparatively little malignancy, so little, in fact, that if this area had been the only one involved, recovery would have been anticipated. It is probable that in many cases peritoneal involvement has existed, given mild symptoms and cleared up. This case is unique in that the child was taken sick on the fourth day of life. This indicates an incubation period of not more than four days. From the description of the mother, the other child who died of an ailment diagnosed meningitis might have died of influenzal meningitis. The parents could not be located for cultures of their noses and throats. The importance of this detail should have been anticipated.

Progress in Pediatrics

DIVERTICULUM OF THE BLADDER IN INFANCY AND IN CHILDHOOD

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Vesical diverticula, although not mentioned in the standard textbooks on pediatrics, constitute a definite clinical entity in childhood which should be borne in mind in cases in which infants and children present urinary symptoms of obscure origin and when there are such evidences of obstruction of the neck of the bladder as the presence of a suprapubic tumor, difficult urination or dribbling.

REVIEW OF THE LITERATURE

The selection of cases from the literature has been somewhat difficult owing to the fact that prior to the present century writers did not use the term "diverticulum" with any degree of uniformity, but employed such terms as "sacs," "bladder compartment" and "double bladder." Furthermore, it is evident that many of these were instances of patent urachus, abscess pockets, encysted calculi or definite developmental anomalies of the lower urinary tract, and not diverticula as conceived today. Moreover, a large number of the early cases were so incompletely reported, and were described in such vague terms that to include them in this study would contribute to a series of misstatements.

Since vesical diverticula are generally a condition of the later years of life, there is little mention made of their occurrence in infants and children in the voluminous literature on the subject. But the statistics of Durrieux and of Englisch showed a surprisingly large percentage of diverticula in persons under 10 years of age. However, owing to the confusion which existed at that period as regards the term "diverticulum," and as shown by a brief survey of the cases described by these authors, the reliability of their statistics is questionable.

Fischer reviewed 48 cases of vesical diverticula collected from the American and German literature, and found that 6 of these were in children under 14 years of age. Wallfield wrote an article "Congenital Diverticula of the Urinary Bladder in Infants and Children." This is

Read before the Billings Medical Club, Chicago, Nov. 7, 1933.

the first contribution which I have found devoted to the special clinical and diagnostic features of vesical diverticula in young persons. He reported 2 cases from his own experience. One was that of a boy, 9 years of age, in whom a fold of mucous membrane hung from the upper part of the left wall of the bladder. From the author's description it does not appear to have been a true diverticulum, and is not so considered by later writers.

Hinman, in an analysis of vesical diverticula reported from 1899 to 1919, found that in 154 cases in which the ages were stated, 18 of the patients were under 30 years and only 7 under 20. The cases which he reviewed in persons under 15 years are those of Handl, Wallfield, Young and Brongersma.

Hyman published a study, "Diverticula of the Bladder in Children," based on 3 cases from his own experience. He was of the opinion that the condition is undoubtedly more frequent in childhood than would be inferred from the scarcity of the reports in the literature, and attributed this to the lack of complete urologic investigation in childhood.

In 1929 Caulk reported an interesting case of the accidental finding of a symptomless vesical diverticulum in a female infant. The diverticular orifice was outside of that of the left ureter. During cystoscopic examination a rhythmic peristaltic movement was observed, at the height of which the ureteral opening was drawn into the diverticulum.

Randall reported the occurrence of a diverticulum in the bladder of a 6 year old child. The interesting feature of this case was that the ureteral orifice was located on the lip of the diverticular orifice. This study was made at autopsy.

I have found reports of 19 cases of diverticula of the bladder in children which appear to be authentic, and which are reported with varying degrees of detail. These are listed in the accompanying table with 2 clinical cases and 4 examined at autopsy which are reported in this paper, making 25 cases of vesical diverticula in infancy and childhood on which to base this study.

AGE AND SEX INCIDENCE

Age.—In a review of the age incidence in the 25 cases of vesical diverticula that form the basis of this paper the following distribution was noted: 1 year and under, 8 cases; from 2 to 5 years, 7; from 5 to 10 years, 7, and from 10 to 12 years, 3.

Sex.—As regards the incidence of sex the following was noted: males, 22 cases; females, 2; not stated, 1. From this it would appear that the occurrence of vesical diverticula in childhood is at least eleven times more frequent in males than in females. My personal series of

TABLE 1.—*Diverticula of the Bladder in Children*

No.	Author	Date	Age	Sex	Symptoms	Duration of Symptoms	Clinical Diagnosis	Method of True Diagnosis	Position and Relation to Ureters	Size	Relation to Obstruction	Associated Pathologic Process	Associated Congenital Anomalies	Treatment	Outcome	Comment
1.	Hayfelder	1859	6 yrs.	M	Those of a stone in the bladder	Not stated	Vesical calculi	Autopsy	Posterior to bladder; relation to ureters not stated	"Larger than bladder"	Not stated	Calculus in diverticulum	None	Cystotomy for vesical calculus; stone was not found	Death, few days postoperative	
2.	Humphry	1864	9 yrs.	M	Those of a stone in the bladder	5 yrs.	Vesical calculi	Operation	Left side	Not stated	Not stated	Vesical calculus	None	Cystotomy with removal of calculus	Death, six weeks postoperative	History dated 1855
3.	Holmes	1864	3 days	M	Swelling of abdomen; hematuria	.....	.....	Autopsy	Not stated	Not stated	Not stated	Bilateral hydronephrosis and hydroureters; hypertrophy of bladder wall	Undescended testicle	None	Death on eighth day	
4.	Zacharisson (quoted by Englisch)	1896	21 mos.	M	Urinary retention	Not stated	Not stated	Operation	Left side; relation to ureters not stated	Not stated	Marked phimosis caused obstruction	Left pyonephrosis; cystitis	Phimosis; reduplication of ureter to left kidney	Suprapubic cystotomy; destruction of the septum between diverticulum and bladder	Death	
5.	Lungren (quoted by Englisch)	1897	12 yrs.	M	Difficulty of urination; abdominal pain	3 yrs.	Not stated	Operation	Behind bladder	Not stated	Not stated	Not stated	Not stated	Suprapubic cystotomy; large opening made between diverticulum and bladder	Cured	
6.	Zacharisson (quoted by Englisch)	1904	8 yrs.	M	Urinary retention	Not stated	Not stated	Operation	Left side; relation to ureters not stated	Not stated	Marked phimosis	Severe cystitis	Phimosis	Operation for phimosis; suprapubic cystotomy with widening of diverticular opening	Cured	

7. Corner and Rowntree	1905	18 mos.	..	Swelling in right side of scrotum	Since birth	Irreducible inguinal hernia	Operation	Not stated	2 inches long	Not stated	Tuberculosis in diverticulum	Inguinal hernia	Excision of diverticulum with Bassini closure of wound	Complete recovery	Diverticulum was in an inguinal hernia
8. Handl	1910	3½ yrs.	M	Painful urination; urinary retention	2 mos. 4 days	Acute appendicitis	Autopsy	Contained right ureteral orifice	Hen's egg	Not stated	Cystitis; pyeolnephritis; hypertrophy of bladder; dilatation of ureters	Not stated	Operated on for acute appendicitis	Death from sepsis 9 days after operation	Symptoms due to a fall
9. Brongersma	1918	12 yrs.	M	Incontinence; painful urination; abdominal pain	9 yrs.	Not stated	Cystoscopic examination	Near right ureteral orifice	5 by 4 by 3 cm.	Not stated	Bilateral hydronephrosis and dilatation of ureters	Not stated	Excision of sac	Death with uremic symptoms 6 days after operation	
10. Wallfield	1915	6 mos.	M	Hematuria; blood in stools; distended bladder; mass palpable by rectum	Not stated	Colic; intestinal intussusception	Operation	Not stated	Not stated	Not stated	Not stated	Not stated	Laparotomy under diagnosis of intussusception	Death from sepsis 6 weeks later	
11. Stern	1918	8 yrs.	M	Acute symptoms	No further details given except that diverticulum was "large"										
12. Young	1918	10 yrs.	M	Pyuria; frequency	8 yrs.	Not stated	Cystoscopic examination	External and posterior to left ureteral orifice	Hen's egg	Not stated	Not stated	Trigon prominent	Excision of diverticulum; division of trigon	Recovery	
13. Fronz	1920	12 yrs.	F	Fever; pain; rigidity of lower part of abdomen	9 days	Acute appendicitis	Operation	Near right ureteral orifice	Larger than goose egg	Not stated	Peridiverticulitis	Not stated	Excision of diverticulum	Recovery	
14. Hyman	1923	3 yrs.	M	Retention; dysuria; enlarged abdomen; cloudy urine	6 mos.	Not stated	Cystoscopic examination, cystogram	Right side contained right ureteral orifice	Small	No evidence	Peridiverticulitis; dilated ureters	Not stated	Excision of diverticulum	Recovery	

TABLE 1.—*Diverticula of the Bladder in Children—Continued*

No. Author	Date	Age	Sex	Symptoms	Duration of Symptoms	Clinical Diagnosis	Method of True Diagnosis	Position and Relation to Ureters	Size	Relation to Obstruction	Associated Pathologic Process	Associated Congenital Anomalies	Treatment	Outcome	Comment
15. Hyman	1923	9 mos.	M	Diarrhea; fever; distention; pyuria	4 wks.	Not stated	Cystogram	2 diverticula; ureters behind sacs on each side	Each size of an orange	No evidence	Left pyonephrosis and pyoureter; stricture of left ureter	Not stated	Excision of sacs	Recovery	Left ureteronephrectomy 7 months later
16. Hyman	1923	9½ yrs.	M	Hematuria; dysuria; pyuria; albuminuria	6 days	Not stated	Cystoscopic examination	Near left ureteral orifice	Large	No evidence	Dilatation of left ureter	Penile hypospadia	Excision of diverticulum	Recovery	
17. Caulk	1929	3 mos.	F	None	.....	.....	Cystoscope	Outside left ureteral orifice			.....*	.....	.....	.....	Rapid recovery
18. Pugh	1929	5 yrs.	M	No details given except that the child had a vesical diverticulum and also spina bifida											
19. Randall	1930	6 yrs.	Not stated	Died in uremic coma	Not stated	Not stated	Autopsy	2 diverticula in relation to both ureteral orifices	Not stated	Not stated	Bilateral hydronephrosis and trabeculated bladder	Bilateral bifurcation of renal pelvis	Not stated	Death	
20. Kretschmer	1931	2½ yrs.	M	(a) Dribbling; (b) chills; fever; suprapubic tumor	(a) Since birth; (b) 4 mos.	Not stated	Cystoscopic examination; cystogram	Near right ureteral orifice	Not stated	Not stated	Trabeculated bladder	Contracture of vesical neck	Excision of diverticulum and resection of internal urethral orifice	Recovery	
21. Kretschmer	1933	20 mos.	M	Suprapubic tumor; mass in region of right kidney	Noted almost 1 mo.	Congenital anomaly of urinary tract with secondary hydro-ureters and uremia	Autopsy	Diverticulum contained in right ureteral orifice	Not stated	Congenital valve in posterior urethra	Bilateral hydronephrosis and hydroureters; cortical abscess of left kidney; bladder hypertrophy; dilatation of posterior urethra	Valve (iris diaphragm) of posterior urethra; double left renal pelvis	No operation	Death 16 days after admission to hospital	

22. Kretschmer	1933	2 mos.	M	(a) Projectile vomiting; (b) abdominal swelling, palpable right kidney, edema of right leg; pyuria; albuminuria	(a) Since birth; (b) 3 wks.	Obstruction of vesical neck	Autopsy	Diverticulum contained in right ureteral orifice	Not stated	Congenital iris valve of urethra	Bilateral hydroureter; pyelonephritis; hypertrophy and dilatation of bladder	Iris valve of urethra	Indwelling catheter and administration of fluids	Death (bronchopneumonia) 2 months after admission to hospital		
23. Kretschmer	1933	12 mos.	M	Fever; diarrhea; loss of weight	1 wk.	Alimentary intoxication	Autopsy	Diverticulum near left ureteral orifice	Small	Not stated	Left hydronephrosis; and hydroureter; hypertrophy of wall of bladder	Fetal lobulation of right kidney	None	Death 16 hours after admission to hospital		
24. Kretschmer	1933	12 days	M	Passed no urine for 60 hours after birth; difficulty on urination; pyuria; albuminuria; suprapubic tumor	Since birth	Congenital obseruction of neck of bladder; hydronephrosis and hydro-ureters	Intravenous pyelogram and autopsy	2 diverticula, 1 contained in right ureteral orifice, 1 near left ureteral orifice	Not stated	Congenital valve in posterior urethra (iris type)	Dilatation of posterior urethra and bladder; left hydronephrosis and hydro-ureter	Aplasia of right kidney and ureter	None	Death a few days later	Before death exfoliative dermatitis developed; neonatorum (Ritter's disease)	
25. Kretschmer	1934	12 mos.	M	Dysuria; retention; pyuria; suprapubic tumor	2 mos.	Congenital obstruction of neck of bladder; vesical diverticula; cystitis	Cystoscopic examination and cystogram	2 diverticula, 1 on right side, 1 on left	Not stated	Congenital obstruction of neck of bladder	Stones in diverticulum	Obstruction of neck of bladder	(1) Resection of diverticula in two sittings; (2) removal of stone from diverticulum; (3) resection of neck of bladder	Recovery		

* Discovered accidentally during the cystoscopic drainage of pyelitis on the right side complicating empyema. The diverticulum evidently caused no symptoms.

vesical diverticula in infancy and childhood occurred only in males. It is my impression that this condition in female children is extremely rare, and occurs probably less frequently than is indicated in this small series of 25 cases. The 2 cases in females recorded in the literature were those of Fronz and of Caulk.

ETIOLOGY

Although the etiology of vesical diverticula has been the subject of a voluminous literature for the past fifty years, the subject is still far from being settled. With rare exceptions few opinions offered by recent authors had not been suggested by the older writers. The theories with regard to the origin of vesical diverticula may be grouped as follows:

1. That they are congenital.—According to this theory vesical diverticula may be formed before birth, but cause no symptoms which call attention to their existence until urinary obstruction or infection occurs. They may be caused by some form of obstruction to the outflow of urine during intra-uterine life—an increased urinary pressure acting on weak spots in the wall of the bladder. Blum noted that among the causes of congenital urinary obstruction may be listed aplasia and atresia of the urethra, phimosis, valves and diaphragms in the posterior urethra, congenital strictures of the urethra, hypospadia, kinks and compression from without.

The opponents of such a theory state that this is not at all the general rule in intra-uterine obstruction to urination, a general distention of the bladder being the common outcome; moreover, in cases of high grade obstruction there are usually a secondary hydro-ureter and hydronephrosis of a degree not compatible with life (Kneise and Schulze). It is of interest to note in the study of the cases of congenital urethral obstruction gathered from the literature (24 cases) and those from Johns Hopkins Hospital (12 cases) that in no instance was diverticulum formation found in the bladder, although the bladder and the upper urinary tract showed evidences of urinary obstruction of long standing. In other words, intra-uterine obstruction alone cannot, in the opinion of these authors, be considered the responsible etiologic factor.

Another conception of the congenital origin of diverticula in the bladder is that they represent aberrant ureteral buds, which might balloon out if an obstruction to urinary outflow occurs. According to other investigators the normal urinary pressure is sufficient to distend the walls.

Belonging to the group of theories advocating a congenital origin of diverticula in the bladder, yet distinctly in a class by itself, is Watson's theory. He demonstrated that in fetal life, owing to variations and inequality of intrapelvic and lower abdominal pressure, ridgelike

elevations may be produced on the inner wall of the bladder. These ridges may grow and anastomose with the opposite wall, forming definite pockets or sacculations.

In the discussion of his findings Watson stated that congenital factors are of the greatest importance in the production of diverticula of the bladder, their clinical recognition occurring with and their dimensions being increased by any factors which would bring about vesical distention or increased activity of the musculature of the bladder. He stated that they are not usually found in early life owing to the fact that their power to produce symptoms and to increase in size is dependent on the supervening of obstructive lesions, and the latter usually occur in adult life.

2. That they are not present at birth but are represented by a muscular weakness in the bladder wall. According to this theory one might say that there is a congenital anlage of the diverticulum. With the development of urinary obstruction these weak spots herniate, or, according to modern German urologists (Auschuetz, Lurz, Blum) who have advocated this theory, when a spot is decidedly weak, the normal force of urination is great enough to cause it to herniate. This theory may be summarized as stipulating a congenital anlage, or a congenital malformation, but an acquired development. It should be noted that places of muscular weakness in the wall of the bladder have been histologically demonstrated by Marsella, while Rose furnished a histologic study demonstrating the presence of unprotected loose fibrous connective tissues in the wall. Targett was of the opinion that the bladder wall is weakened at the points of entrance of the larger arteries.

3. That they are of acquired origin. One of the strongest advocates of this theory is Hinman who said that he found no clinical or anatomic evidence for the idea that diverticula are congenital. He presented an interesting discussion of the three "factors"—anatomic, pathologic and mechanical—which he believed responsible for the formation of diverticula. Hinman said that generally the whole structure of the wall of the bladder in the presence of a diverticulum is what one would expect in a local herniation which takes years to develop.

OBSTRUCTION

In the largest number of cases of diverticulum of the bladder in adults careful search is rewarded by the discovery of an obstruction at the vesical orifice or deep in the urethra, that is, the presence of valves. In a few instances diverticula are found associated with long-standing neglected strictures of the urethra. Cases without obstruction are rare and raise the question of the possibility of some overlooked lesion of the

central nervous system; but again, these are the exception. It would appear, therefore, that in the largest majority of cases, if not in all, obstruction to the outflow of urine is a common accompaniment of diverticulum.

The fact that an obstruction is present does not mean that diverticula must necessarily follow; that is, although diverticula in adults are associated with benign hypertrophy of the prostate, not every case of benign hypertrophy of the prostate is associated with a diverticulum. There may be some other, as yet unrecognized, factor that is not present in each case.

Of great interest are the 3 cases in children reported by Hyman, who noted that there was no evidence of obstruction in the lower portion of the urinary tract. He stated that the finding of vesical diverticula in young patients, without evidence of obstruction, would lead one to conclude that they are congenital and that many diverticula in adults have the same origin.

Relation to Diverticula.—The relationship between diverticula and obstruction is an important phase of the subject and one that bears repeating. As a rule, when evidence of obstruction is searched for, it is found. When no mechanical evidence can be demonstrated, a careful examination of the central nervous system may reveal some underlying neurologic condition. Occasionally even this may be normal.

It is unfortunate that in the older reports of cases there is no mention of the relationship between diverticula and obstruction. This was probably due to the fact that the relationship was not recognized and hence not looked for.

A review of the 25 cases in this series showed the following: marked phimosis, 2 cases; congenital valves of the posterior urethra, 3 (Kretschmer); congenital contracture of the vesical neck, 2; no obstruction of the lower part of the urinary tract, 4; not stated, 14.

SYMPTOMS

Diverticula in adults do not, as a rule, present symptoms so characteristic that the condition can be readily recognized. It is generally discovered during the course of a clinical examination; that is, during the course of a cystoscopic examination the opening of a diverticulum is seen (or several may be present). However, the fact should not be lost sight of that it is relatively easy to overlook the opening of a diverticulum during a cystoscopic examination, especially in case of severe cystitis. On the other hand, the routine use of cystography often shows the presence of a diverticulum when least suspected. Moreover, by means of the routine use of intravenous urography unsuspected cases in

children are disclosed—cases which otherwise would have been overlooked. The absence of a typical symptom complex, coupled with the fact that it is often hard to get an accurate history and a thorough account of subjective symptoms in infancy and early childhood, accounts for the fact that this condition is so frequently overlooked in children.

The presence of a persistent suprapubic tumor, the demonstration of residual urine and pus in the urine and a history of long-standing dribbling should arouse one's attention to the possibility of the presence of a diverticulum.

The following symptoms were noted in a review of the record of the 6 cases which form the basis of this paper: suprapubic tumor, 5 cases; pyuria, 3; painful urination, 2; chills, fever, vomiting, 1; dribbling, 1; restlessness, fever, diarrhea and loss of weight (no urinary symptoms), 1; retention, 1; difficult urination, 1; albuminuria, 1, and edema of the left leg, 1.

The duration of the symptoms seems to be variable. This is due to the lack of observation on the part of the parents or nurse and also to the fact that mild symptoms of chronic obstruction are masked by the acute onset of nausea, vomiting, chills and fever. Thus, in the 6 cases herein reported the following duration of symptoms was noted:

In the first case, in a boy, 2½ years old, dribbling was present since birth. Acute symptoms—chills, fever and vomiting, with distention of the bladder—were of four months' duration. In the second case, in a 20 month old boy, a suprapubic tumor reaching over ½ inch (1.27 cm.) below the umbilicus and cramplike pains at the beginning of micturition were evident for one month, after which death occurred suddenly. In a third case a 2 month old boy had shown projectile vomiting shortly after feeding since the twelfth day, with an enlargement of the abdomen, a palpable right kidney and pus in the urine of three weeks' duration. In the fourth case a boy of twelve months showed restlessness, fever, diarrhea and loss of weight, with no urinary symptoms, while a physical examination gave negative results. This case was of brief duration, the child dying one week after the onset of symptoms and sixteen hours after admission to the hospital. In the fifth case a male infant of 10 days had shown retention of urine and the bladder had been distended to a fingerbreadth below the umbilicus since birth. In the sixth case a 12 month old boy showed the symptoms of painful urination, distention of the bladder to one fingerbreadth above the umbilicus and pus in the urine of two months' duration.

Duration.—In the review of the 25 cases listed in the table the duration of symptoms varied from six days (Hyman) to nine years (Brongersma). The symptoms in Stern's case were merely described as "acute." There were no symptoms in Caulk's case, and the symptoms were not given in 7 cases. The duration of symptoms noted was as follows: one year or less, 11 cases; from one to three years, 2; from five to six years, 1; eight years, 1; nine years, 1; no symptoms (Caulk), 2; not stated, 7.

ASSOCIATED PATHOLOGIC CHANGES

Because of the association of diverticula with obstruction at or in front of the neck of the bladder, certain changes occur in the bladder and upper part of the urinary tract which are commonly associated with diverticula. These changes form a definite and constant finding, depending on the duration of the underlying obstructive factors. In the cases in which a diverticulum is recognized early these changes are often slight or may be absent, whereas later in the course of the disease they are constant and are often developed to a marked degree. Besides these changes, others may occur in the diverticulum itself, and not infrequently they spread beyond the sac, and peridiverticulitis is found.

A review of the cases collected from the literature, as well as my own (tabulated here), shows a surprisingly large number of associated pathologic conditions. In some of the early cases in the literature exact details are absent or are not stated clearly, yet one is surprised, even in the face of incomplete reports, to see how common associated lesions are. They may be conveniently divided into the following groups: 1. Changes in the diverticulum took the form of calculus in the diverticulum in 2 cases, marked peridiverticulitis in 2 and tuberculosis in the diverticulum in 1. 2. Associated pathologic changes in the bladder appeared as contracture of the neck of the bladder in 2 cases, as marked hypertrophy of the wall of the bladder neck with trabeculation in 8, as severe cystitis in 4 and as stone in the bladder in 1. 3. Associated changes in the urethra appeared as congenital valves in the posterior urethra in 3 cases, and as marked dilatation of the posterior urethra in 1. 4. Associated changes in the upper portion of the urinary tract were unilateral hydro-ureter in 8 cases, bilateral hydro-ureter in 5, unilateral hydronephrosis or pyonephrosis in 7 and bilateral hydronephrosis or pyonephrosis in 5.

It is evident that in all these cases there was definite dilatation in the upper part of the urinary tract, and in some infection occurred.

Associated Congenital Anomalies.—It is a well recognized fact that not infrequently in cases of congenital anomalies more than one anomaly may be present. A review of this series shows the presence of a large number of associated congenital anomalies. No doubt in some of the early cases some of the anomalies were either not recognized or, if recognized, not included in the reports of cases. For example, in some of the cases reported before routine cystoscopic and pyelographic study was done, or before complete studies were made at autopsy, some anomalies in the kidneys may have been overlooked.

The following congenital anomalies were reported, the renal anomalies predominating: congenital anomalies of the kidney and ureters, 5 cases (1 showing aplasia of the right kidney and ureter; 1, reduplica-

tion of the ureter to the left kidney; 1, bifurcation of the renal pelvis; 1, a double pelvis of the left kidney and 1, a fetal lobulation of the right kidney); valve of the posterior urethra, 3; contracture of the vesical neck, 2; phimosis, 2; inguinal hernia, 1; penile hypospadia, 1; spina bifida, 1; undescended testicles, 1, and "prominent trigon," 1 (Young). Thus, in a series of 25 cases of diverticula in the bladder in infancy and childhood, there were 17 definitely congenital associated anomalies. In one of my own cases the diverticulum was associated with a posterior urethral valve and a double left renal pelvis. Marked phimosis and reduplication of the left ureter were found in the case of Zacharisson (quoted by Englisch).

DIAGNOSIS

At present there is no excuse for deferring adequate and complete urologic investigation in all cases of persistent urinary symptoms in infants and children. It is a well known fact that infants and children stand urologic examination as well as adults, or even with less reaction, so that cystoscopy and ureteral catheterization may be carried out with impunity even in the youngest child.

The diagnosis of vesical diverticula in the child is best made by cystography and cystoscopy, as in older patients. The fact that vesical diverticula are seldom considered in childhood is due to failure to recognize them. As previously mentioned, diverticula are often found during a cystoscopic examination when least suspected. In certain instances cystoscopy may be difficult; as for example, in the presence of marked pyuria, when it may be impossible to clear up the bladder sufficiently to give a clear picture. Although cystoscopy gives the site of the diverticular orifice, it does not give information about the size or shape of the sac. It is also possible to overlook a small orifice.

Cystography, on the other hand, is such a simple procedure that it may be used even in the very young. If cystoscopy and ureteral catheterization are feasible, a roentgen catheter should be introduced into the ureter and another into the sac so as to outline the position of the sac with relation to the ureter. In making cystograms it is desirable to take lateral as well as anteroposterior exposures, since small diverticula may be hidden behind the outline of an unusually large shadow of the bladder. On account of its simplicity and relative freedom from danger, a routine cystogram should be made in every patient with a history of urinary obstruction of long standing with chronic pyuria.

I have never seen bad results or effects following cystography in infants and children. I generally use a 5 per cent solution of sodium bromide. The solution is first warmed to body temperature and then allowed to run into the bladder slowly and without force.

Although exceedingly rare, the possibility of vesical diverticula should be considered in every case in which fibrosis of the vesical neck or other forms of obstruction to the outflow of urine (hypertrophy of the verumontanum, congenital valves of the posterior urethra, etc.) are diagnosed. If the diverticulum is large, neglect in removing it may result in failure to relieve the patient of his symptoms when treatment

A cystogram showing the presence of a large diverticulum that fills the iliac fossa and reaches to the level of the second lumbar vertebra. At operation the diverticulum was much larger than the bladder itself (case 25).

is carried out to relieve the obstruction. On the other hand, when diverticula are discovered in childhood, an obstruction of the lower part of the urinary tract should be sought and, when found, as is nearly always the case, it should be adequately treated.

Similar to every form of urologic surgery, a study of renal function is imperative preliminary to the operation for vesical diverticula. In cases of greatly distended bladders, due to large amounts of residual

urine and with poor renal function, preliminary drainage of the bladder with gradual decompression must be done.

The potential danger is great in some children. As is well known, catheterization of a patient with prostatic obstruction who has had a chronic residual condition for many years and who has as yet no infection of the urine, carries with it the dangers of infection of the bladder with acute pyelonephritis and occasionally death. The same danger is present in infants and children; therefore, the greatest care must be exercised when catheterization is carried out. The question often arises whether it would not be better to use cystostomy instead of repeated catheterizations or an indwelling catheter.

When the symptoms are acute and sudden in onset with no special reference to the urinary tract, the diagnosis of vesical diverticula is especially confusing. In Frontz's and in Handl's patients the diagnosis established was appendicitis, and an operation followed; in Wallfield's case the condition was diagnosed as intestinal intussusception and operation was performed. Two of Hyman's patients were treated for pyelitis. The condition of one of my patients, who presented no urinary symptoms, was diagnosed as alimentary intoxication.

TREATMENT

Radical extirpation is the rational treatment for vesical diverticula in children as well as in adults. It is well to bear in mind that in almost every case there is an associated lesion producing obstruction at or in front of the internal urethral orifice and that unless this obstruction is removed, failure is bound to result. The necessity for an accurate preoperative diagnosis in each case is obvious.

During the course of the operation great care must be exercised in establishing the relationship between the diverticulum and the ureter in order to avoid injury to the ureter during the isolation or removal of the diverticulum. At times this is a difficult task. One may simplify this by inserting a ureteral catheter or bougie into the ureters through the open bladder, or the ureter may be isolated above the diverticulum, opened by an incision and the catheter passed down the ureter into the bladder. The general opinion seems to prevail that in a large number, or perhaps in the majority of cases, the ureter and diverticulum are in close association. That this general impression is correct is evident from the fact that in the 20 cases in this series in which the location of the diverticulum is given, 15 were in definite relation to the ureters, as follows: in relation to a right ureteral orifice, 7 cases; in relation to a left ureteral orifice, 4; two diverticula in relation to the right and left ureteral orifices, respectively, 4; posterior to the bladder, with the relation to the ureters not stated, 2; on the left side, the relation to ureters

not being mentioned, 3; position not stated, 5. In the adult the frequency with which the opening of the diverticulum is located near the ureteral orifice is well known; this is so striking that it has been emphasized by many observers.

It is needless to state that a preliminary study of the renal function must be made in every case and that no operation should be done until the renal function has been improved and stabilized. Infection, when present, should be treated with the indwelling catheter and irrigations; in some cases a suprapubic cystostomy is necessary. Great care should be exercised in the management of the noninfected patient with a large amount of residual urine.

PROGNOSIS

In view of the fact that children stand major operative procedures well, it may be stated that the prognosis is favorable in uncomplicated cases of vesical diverticula which come to operation before the kidneys are severely damaged. Owing to the tendency of vesical diverticula to be complicated with other congenital anomalies, it stands to reason that the prognosis is more favorable in uncomplicated cases.

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Pediatric Biographies

DANIEL WHISTLER

1620?-1684

A NOTE ON THE HISTORY OF RICKETS

JOHN RUHRÄH, M.D.
BALTIMORE

Perhaps the first account of rickets is in the book of Soranus written when Trajan ruled in Rome. It seems strange that the disease could have escaped description as long as it did after that, but this may have been due to the fact that it was common, rather than uncommon. In 1582 Jerome Reussner, in a disputation at Basle, described rickets as a disease of children, common in Holland and Switzerland. He noted the weakness and the deformities of the chest and legs. Then the matter rested until 1645, when Daniel Whistler presented a thesis at Leyden entitled "De morbo puerili Anglorum, quem patrio idiômate indigenae vocant The Rickets." This was printed in Leyden by Wilhelm Christian Boxius.

Daniel Whistler was born in Essex, at Walthamstow, and he uses the term *Anglo-Saxonicus orientalis* in describing himself. He was sent to the Free School in Thame, Oxfordshire, and in 1639 entered Merton College, Oxford. After receiving the degree of Master of Arts in 1644, he went to Leyden to study medicine and was graduated Doctor of Medicine in 1645. On his return to England, on the strength of his doctor's degree, he was incorporated Doctor of Medicine at Oxford. This was in 1647. He was made a fellow of the College of Physicians in 1649. In 1653 he went as physician to the embassy in Sweden and on his return took an active part in the management of the college.

He was Harveian lecturer in 1659, served twelve times as censor and was also registrar for some years. In 1682 he was made treasurer, and during the next year he was elected president. In all of these positions he was seemingly negligent, and some claim even worse things. Various writers have commented on this, notably Munk and Norman Moore. George Still, on the other hand, puts in a good word for Whistler and thinks that he was careless rather than criminal. Although he married a wealthy woman and is supposed to have had a practice of some £1,000 a year, he died in debt in 1684. Whistler was some-

thing of a politician and enjoyed the friendship of Oliver Cromwell. In 1663 he became a fellow in the Royal Society. He was immensely popular. On the occasion of his receiving his medical degree a volume of six poems in Latin was published by his friends. There is a copy in the Bodleian Iibrary entitled "Plausus congratulantes in honorem ornatissime viri D. Danielis Whistler." He used to sup frequently at the Crown Tavern with fellows of the Royal Society after their

Fig. 1.—Whistler's portrait in the Royal College of Physicians, London.

meetings. He met many noted men, among them Robert Hooke, who told Samuel Pepys of the successful transfusion experiment on dogs, and of this Pepys wrote in his diary, "and doubts not its being found of great use to man; and so Dr. Whistler, who dined with us at the tavern." Pepys also mentions him on Feb. 4, 1660. "We sat late, talking with my Lady and others and Dr. Whistler, who I found good company and a very ingenious man: so home and to bed." Evelyn also mentions him as "the most facetious man in nature."

In his will, made the day before he died, Whistler left the College of Physicians some of his property.

Whistler's book is rare; in fact, even in England it was for a long time known only by such writers as Munk and Norman Moore and in the reprint of 1684, which Whistler had made shortly before he died, while he was president of the college. Some doubted the actual existence of the edition of 1645, but William Munk found a copy in the college library in a cupboard. The title page bears the cut of a bird trying

DISPUTATIO MEDICA INAUGURALIS, DE Morbo puerili Anglorum, quem patrio idiômate indigenæ vocant The Rickets, QVAM Deo ſuppetias ferente, Ex authoritate Nobiliſſimi Domini Rectoris Magnifici, D. JOHANNIS POLYANDRI à KERCHOVEN SS. Theologiæ Doctoris, ejuſdemque Facultatis in Illuſtriſſimâ Acad. Lugd. Bat. Profeſſoris primarii, Decreto Illuſtriſſimæ Facultatis Medicæ, & Ampliſſimi Senatûs Academici conſenſo, Pro Gradu Doctoratûs, ſummiſque in Medicinâ Privilegiis conſequendis, Diſcutiendam proponit DANIEL WHISTLER, Anglo-Saxonicus-Orientalis. Ad diem 18. Octob. Horis & Loco conſuetis.

LUGDUNI BATAVORUM, Ex Officinâ WILHEMI CHRISTIANI BOXII. 1645.

Ob defectum exemplarium novis typis conſcribendum hoſce Theſes Author vulgat.

Londini, Ex Typis Thomæ Flesher, 1684.

DISPUTATIO MEDICA INAUGURALIS, DE Morbo puerili Anglorum, quem patrio idiômate indigenæ vocant The Rickets, QVAM Deo ſuppetias ferente, Ex authoritate Nobiliſſimi Domini Rectoris Magnifici, D. JOHANNIS POLYANDRI à KERCHOVEN SS. Theologiæ Doctoris, ejuſdemque Facultatis in Illuſtriſſimâ Acad. Lugd. Bat. Profeſſoris primarii, Decreto Illuſtriſſimæ Facultatis Medicæ, & Ampliſſimi Senatûs Academici conſenſo, Pro Gradu Doctoratûs, ſummiſque in Medicinâ Privilegiis conſequendis, Diſcutiendam proponit DANIEL WHISTLER, Anglo-Saxonicus-Orientalis. Ad diem 18. Octob. Horis & Loco conſuetis.

LVGDVNI BATAVORVM, Ex Officinâ WILHEMI CHRISTIANI BOXII. 1645.

Fig. 2.—Title pages of both editions of Whistler's book.

to swallow what looks like a horseshoe, of which Norman Moore remarks, "The bird's supposed power of digesting iron now seems to have made the Dutch book sellers think it an appropriate symbol of the capacity for assimilating knowledge in its toughest forms."

Whistler made no claim of discovering the disease, nor does it appear that he had made any extensive clinical or pathologic study, but the fact remains that it is the first description of rickets by an Englishman. He suggested the name "paedosteosplanchnosteocace." He states that the name rickets is said by some to have been given to the condition

by those who treated it empirically, and that it is said by others to be an adaptation of the Dorset dialect "to rucket," meaning to breathe with difficulty, because that symptom may be met with in rickets. He starts off with the diagnostic signs as follows:

1. First one observes an unnatural distension of the hypochondria, or an undue swelling of the abdomen with some hardness, especially in the right side under the liver.

2. The epiphyses at the joints are larger than the age would warrant and there is a disparity in size compared to the rest of the body, especially the arms and feet, from which symptoms some distinguish the whole disease by the name Paedarthrocaces or Paedarthronicias.

3. Nodosities also grow out on the sides [of the chest] where the cartilages join the bones.

4. The whole osseous system is flexible, very like semi-fluid wax, so that the flaccid and enervated legs can scarcely systain the incumbent body, so that the tibias succumb to the weight of the fabric pressing down from above, and from the same cause the thighs above are curved, and the back on account of the bending of the spine presents a gibbosity in the lumbar region so that they cannot sit erect, much less stand when the disease is increasing. From these symptoms some name this affection, Paedosteocaces.

5. These [children] have an increase in the size of the head, sometimes too with hydrocephalus, from which happening some wish not unjustly to call the whole disease, Paedocephalarthroncias.

6. In the soft parts of the skin, flesh, ligaments, etc., there may be noticed a weakness and flabbiness unsuited to the age.

7. The teeth are cut late and with difficulty and often when they appear, they decay.

8. There are concomitantly narrowness of the chest, a sharp pointed sternum, and asymmetry, sometimes of the whole sternum, especially towards the ensiform cartilage [mucronatam cartilaginem], which is depressed, drawn inwards to the osseous ends of the ribs, this often happens in the beginning.

9. Respiration is perceived to be difficult at last, sometimes with a little cough and wasting.

10. In this disease there is often an accompanying slow fever, irregular, of no certain type and erratic temperature.

11. The pulse of the patient is uneven and weak.

12. The urine is thicker than normal, often varying in color and consistence as in scurvy.

13. Sometimes diarrhea and vomiting may supervene and the ejected excrement is viscid and phlegmy.

14. The appetite is either moderate or poor; sweets, such as sugar, are little relished.

15. They sleep moderately, if not too much, unless something prevents.

16. As to disposition they are often bright and of precocious mind, so that from this superstitious parents may predict unfavorably as to their longevity. They do not enjoy play much but are serious beyond their years; but those with hydro-

cephalus are duller because the brain is oppressed with much water or phlegm. They are slow to anger and [not inclined] to irritability; love quiet and are rather slow in movement.

17. Sometimes there are pustules and blotches on the face, chest and limbs resembling scurvy or venereal disease according to whether this or that disease is to be suspected in the parents, grand parents or great grand parents.

The rest of the symptoms which sometimes, but rarely, accompany we do not consider worthy of recital inasmuch as they may arise from the type of bodily constitution or the complications of some other affection. . . .

The definition of the disease is as follows:

Paedosplanchnosteocace is a disease of the bone and viscera in early life, is a children's disease which affects all the viscera and boney structures on account of irregular composition of the blood. As a result of it the fibrinous part of the blood is impacted in the viscera, gets stuck and blocks them up, while the serous part is thrown out into the tissues of the body, or stagnates in the cavities of the body. As a result the abdomen swells. The joints of the wrists and ankles become swollen in spots, cartilaginous nodes arise in the ends of the ribs. The whole boney structure becomes waxy and flexible. The head usually enlarges in size. The soft parts become relaxed. At first the sternum is depressed, but as the disease progresses it projects and this is accompanied by dyspnea and a slow fever.

There are in all twenty-one short parts.

In part V Whistler makes a few observations on what is thought to be the nature of the disease. He states that a most learned man had advanced the opinion that the condition is due to the fact that the nutritive juices do not penetrate the bones because the density is too great. Whistler does not think that this is the case. In part VI he discusses the pathology and thinks that the changes are due to too much serous fluid in the epiphyses, which makes them swell, and that the viscera become enlarged from getting too much of the thick nutritive part of the blood. In part XI he defines the disease in eight lines in italics, a restatement of what he has previously set down.

Part XVI deals with the prognosis:

1. Those who have the disease from birth or before all die. This is a sign that the powerful cause of the disease has invaded so quickly that the nature of those so young is not sufficiently strong to throw it off.

2. More of the female sex suffer but these more quickly and certainly convalesce.

3. Those with hydrocephalus which separates the sutures die.

4. Those who bear movement of the body best recover most easily.

5. Those whose feet are affected are cured most easily, and those who are older.

6. Where the head can scarcely be held on the neck cure is rare; also those with great difficulty in breathing. With suppuration of the lungs never.

7. A small unequal and rapid pulse, especial a weak one [is a bad sign].

There are two and a half pages of treatment suggesting all sorts of drugs. This section is numbered XVII and evidently XVIII, XIX and XX, as the next part is numbered XXI.

Mrs. Alfred Hess, New York, permitted me to use a photostatic copy of the edition of 1645, which Dr. Hess had made in England.

Pediatrics in Art

HELIOTHERAPY

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The modern use of sunlight as a cure and preventive of rickets and for invigorating the system is no new thing, as witness the charming family scene in which Ikhnaton and his wife, Nefteriti, are giving their three infant girls a sun bath. Owing to abundant sunlight, there was no rickets in ancient Egypt. Ikhnaton, before he changed his name, was Amenhotep IV of the Eighteenth Dynasty and ruled prior to about 1350 B. C., seventeen years in all, during which he threw out Ammon and all the old gods and became a sun worshiper. The illustration is a mute witness to the truth of the old saying of Solomon that under the sun there's nothing new. Ikhnaton was a sun worshiper for religious purposes, but two of the girls shown in the second illustration give witness to how the sun god blessed them. The picture is a bas-relief, a slab sculptured *en creux,* now in the Berlin Museum.

Ikhnaton and his wife sunning their children. (Courtesy of the Pratt Library, Baltimore).

The daughters of Ikhnaton. Note the absence of any signs of rickets. (Courtesy of Miss Eleanor Fair and the Metropolitan Museum of Art, New York.)

Correspondence

THE INHERITANCE OF SYPHILIS

To the Editor:—In looking over the June 1929 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN (vol. 37, p. 1283), I observed the statement that congenital syphilis is invariably aquired from the mother. The following facts present presumptive evidence to the contrary.

There is no syphilis in my family (father, mother and ten brothers and sisters) so far as I have discovered, although no exact tests were made. My sister, Mrs. M. L. A., was born in 1839 and married in 1855. Her husband died of scrofula in 1861. At that time, in Oregon, a diagnosis was not scientifically made. The first child of this family, a boy, used crutches for a number of years and died of scrofula at the age of 8. The second child, a daughter, never bore any children. She is alive now, aged 75, and has had fairly good health all these years.

The third child, a son, was a hearty boy and young man. He married at the age of 24 and had three children. When about 50 years of age he acquired arthritis of the knees, wrists and hands. Within three or four years he became helpless, but he lived four or five years longer, becoming blind two or three years before his death. No Wassermann test was ever made. His first born, a son, fell from a sled when 8 years of age, and a swollen and painful knee developed. The condition was diagnosed as tuberculous, and the child was treated for about a year by his physician and by a surgeon of Portland, Ore., although there was no great improvement. The boy was on crutches part of the time and he used them continuously from the age of 15 until he was entirely incapacitated by arthritis of the large joints and of some of the smaller joints, which confined him to his chair and bed for five or six years prior to his death at the age of 33. His second child, a girl, married and has three children, from 8 to 13 years of age, and all are in good health. His third child, a boy, very robust, became afflicted with arthritis when about 21 years of age, becoming helpless within five or six years and dying after three or four years of helpless invalidism. A Wassermann test of this boy gave a positive reaction, but he had never acquired syphilis so far as he was aware. The mother of the men who died of arthritis—that is, the wife of the third son referred to at the beginning of this paragraph—is alive and well at the age of 75. She has had a lifetime of unusually good health without any signs or symptoms of syphilis.

Mrs. M. L. A. married a second time. A girl was born who died of acute rheumatism at the age of 17. Her health previously had been of the very best. The mother married a third time and raised eight additional healthy children. She is now alive at the age of 95 and has never had any syphilitic symptoms.

To my knowledge, tuberculosis never afflicted any family in the way in which this one was afflicted. All of these deaths, grandfather, father and sons, must have been due to hereditary syphilis. None of them ever acquired syphilis so far as could be ascertained.

H. S. GODDARD, M.D., Portland, Ore.

News and Comment

SOCIETY NEWS

International Association of Preventive Pediatrics.—The fourth conference of the association was held at Lyons, France, on Sept. 27 and 28, 1934, under the presidency of Dr. G. Mouriquand. Among the subjects mentioned for discussion in the agenda are the prophylaxis of malaria in childhood and the prophylaxis of rickets and spasmophilia.

Congress of French Speaking Pediatricians.—The Eighth Congress of French speaking pediatricians was held at Paris on July 9 to 11, 1934.

UNIVERSITY NEWS

The executive committee of the medical faculty, University of Paris, has appointed Dr. B. Weill-Hallé director of the school of puericulture.

Dr. Alfred Friedlander has been appointed dean of the University of Cincinnati College of Medicine.

Dr. Otto Ulrich of the University of Munich has been made an extraordinary professor and placed in charge of the Kaiserin Auguste-Victoria Haus in Charlottenburg.

Dr. Albrecht Peiper of the University of Berlin has been named director of the pediatric clinic at the University of Bonn.

Dr. Volkers has been named physician in chief at the children's hospital at Gelsenkirchen.

DEATHS

Dr. Frederick W. Belknap, for many years a pediatrician in Chicago, died of cerebral hemorrhage on July 16 at the age of 66.

Prof. Paul Reyher, the well known professor of pediatrics at the Kaiserin Auguste-Victoria Haus in Charlottenburg, died suddenly on June 15.

Dr. Durando Durante, for many years editor of *La Pediatria,* died recently in Naples.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

INFLUENCE OF EXTRACT OF ANTERIOR PITUITARY ON AUTOTRANSPLANTED AND HOMEOTRANSPLANTED THYROID. MARTIN SILBERBERG, Arch. Path. **17**:381 (March) 1934.

Injections of extract of the anterior lobe of the pituitary gland produced hypertrophic and hyperplastic changes in the normal and also in the autotransplanted and homeotransplanted thyroid gland of the guinea-pig. The preservation of the homeotransplanted thyroid tissue was considerably improved after the injections. The resting normal thyroid gland was found more suitable for transplantation than a hypertrophic thyroid gland previously stimulated by pituitary extract.

LEMASTER, Evanston, Ill.

A COMPARATIVE STUDY OF THE ANTIDOTAL ACTION OF PICROTOXIN, STRYCHNINE AND COCAINE IN ACUTE INTOXICATION BY THE BARBITURATES. A. H. MALONEY, J. Pharmacol. & Exper. Therap. **49**:133 (Oct.) 1933.

It has been shown clinically as well as experimentally that the barbiturates are effective antidotes against strychnine and cocaine poisoning. The author here shows that picrotoxin and, to a lesser degree, strychnine and cocaine are effective against the toxic action of the barbiturates in rabbits.

In severe poisoning by barbiturates, strychnine and cocaine may hasten death by adding to the respiratory failure; picrotoxin seems relatively free from this danger, and its use was followed by the return of respiration in an animal the heart of which was still beating. Eleven barbiturates were studied.

PILCHER, Cleveland.

THE SITE OF THE ANTIDIURETIC ACTION OF PITUITARY EXTRACT. W. W. BURGESS, A. M. HARVEY and E. K. MARSHALL JR., J. Pharmacol. & Exper. Therap. **49**:237 (Oct.) 1933.

The antidiuretic action of ordinary therapeutic doses of pituitary extract in man and in the dog is due to increased reabsorption of water by the renal tubules. This typical action is also found in the bird, but pituitary extract can here also decrease the quantity of glomerular filtrate. The extremely marked antidiuretic effect obtained in the reptile is entirely due to a marked decrease in glomerular filtrate. No antidiuretic effect was found in amphibians or in fish.

Since the typical antidiuretic effect is found only in mammals and birds in which the loop of Henle is present, the conclusion appears justified that the antidiuretic action of pituitary extract in man (and other mammals) is due to stimulation of reabsorption of water by the thin segment of the loop of Henle.

AUTHOR'S SUMMARY.

ON THE ABSORPTION OF INSULIN FROM THE INTESTINAL TRACT. DAVID CAMPBELL and THOMAS N. MORGAN, J. Pharmacol. & Exper. Therap. **49**:450 (Dec.) 1933.

The authors show that insulin injected into the portal system of the rabbit is as effective as when it is introduced into the systemic circulation. As it is but slowly destroyed in the alimentary canal, they conclude that failure of absorption is the cause of insulin's inactivity when given by mouth. Insulin combined with

lecithin, which makes it lipoid-soluble, was inactive when given by mouth but active on subcutaneous injection; the compound was also inactive when given per os to a nondiabetic human subject.

PILCHER, Cleveland.

AN EXPERIMENTAL INVESTIGATION ON THE TREATMENT OF TOXEMIA. G. NORMAN MYERS, J. Pharmacol. & Exper. Therap. **49**:483 (Dec.) 1933.

The author shows that peripheral vascular paralysis is the cause of shock in diphtheria toxin poisoning. Splanchnic stimulation has no effect; the action of epinephrine is weak, and second doses may be ineffective in raising the blood pressure. This toxemia was best combated by the slow intravenous injection of saline solutions with the addition of alcohol or dextrose or, especially, acacia-saline solutions. (The beneficial action of solutions of dextrose [10 per cent] in diphtheria toxemia was shown some years ago by Edmunds.) Abdominal pressure also improved the circulation by increasing the flow of blood to the heart.

PILCHER, Cleveland.

MICRODETERMINATION OF SODIUM IN BLOOD PLASMA AND IN BLOOD SERUM: SALIT'S MODIFIED TECHNIC. A. D. MARENZI and R. GERSCHMAN, Rev. Soc. argent. de biol. **9**:381 (Oct.) 1933.

Marenzi and Gerschman describe a technic for the microdetermination of the sodium in the blood plasma and in the blood serum. The technic, which is a modification of Salit's method (New Triple Acetate method for Sodium Determination in Biologic Materials, *J. Biol. Chem.* **96**:659 [June] 1932) is based on the precipitation of sodium as a triple salt, its redissolution in water and the formation of uranyl ferrocyanide, which is compared by the colorimetric method. The results obtained with the modified technic are much more exact and coordinated than those obtained with the original technic.

Nutrition

THE INCISOR TEETH OF ALBINO RATS AND GUINEA-PIGS IN VITAMIN A DEFICIENCY AND REPAIR. S. B. WOLBACH and PERCY R. HOWE, Am. J. Path. **9**:275 (May) 1933.

The initial effect of deficiency in vitamin A on the incisor teeth of rats and guinea-pigs is on the enamel organ. The ameloblasts respond earliest by atrophy, then the remainder of the organ atrophies; finally, metaplasia and calcification and, in the guinea-pig, ossification occur. Atrophy and depolarization of odontoblasts follow changes in the enamel organ. The odontoblasts survive longest on the side (labial) in apposition to the enamel organ. In long continued experiments gross deformities in the incisors of rats resulted from absence or deficiency of dentine formation. Two types of denticle formation are described—one in which denticles are built up by depolarized odontoblasts, the other in which they are formed by inclusions of ameloblasts by the folding of imperfectly formed dentine at the formative end of the tooth.

Defective formation of enamel and other poorly understood conditions in teeth, such as denticles, pulp bone and cemento-exostoses, may reasonably be regarded as possibilities in vitamin A deficiency in man. Our observations indicate that in the incisor teeth of rodents the odontoblasts are influenced by the enamel organ throughout life.

As in other morphologic problems concerning vitamin deficiencies, study of the sequences of repair was essential. We emphasize the importance of two types of control material, the normal and the progressive stages in repair.

Our observations indicate that deficiency in vitamin A is the most important of the known vitamin deficiencies in its effect on the formation of teeth.

AUTHORS' SUMMARY.

COMMON SENSE IN INFANT FEEDING. WILLIAM M. HAPP, J. Pediat. **3**:772 (Nov.) 1933.

Feeding babies by following specified tables is condemned. Happ believes that stereotyped methods of feeding infants are unsound and unphysiologic and responsible for a great deal of the crying and anorexia seen in infants. If the concentration of the milk formula is satisfactory, the amount of milk given at a feeding should depend on the appetite of the infant. Only by adjusting the feedings to suit the individual infant can the best results be obtained.

LEMASTER, Evanston, Ill.

VITAMIN D MILK. EDWIN T. WYMAN, New England J. Med. **209**:889 (Nov. 2) 1933.

Wyman reviews the clinical evidence thus far available for appraising the antirachitic potency of vitamin D milk. Laboratory experiments showed this milk to contain approximately 160 units of vitamin D per quart. The potency of vitamin D milk is expressed in terms of the Steenbock unit, which is defined as the total amount of vitamin D which, fed over a ten day period, will produce a narrow, continuous line of healing, termed "a 2 + line."

The administration of antirachitic vitamin in so palatable a form with the automatic prevention of the occurrence of rickets relieves the physician of anxiety as to how much and what antirachitic agent to give. Vitamin D (yeast, 160 units) milk, while it prevents and cures rickets, can do no harm and should be given during the summer months as well as during the winter months in the latitude of Boston. Further investigations should be made to draw a reliable comparison between the efficacy of activated milk and that of yeast milk.

GENGENBACH, Denver.

PRESERVATION OF HUMAN MILK. PAUL W. EMERSON, New England J. Med. **209**:893 (Nov. 2) 1933.

In a previous report it was shown that milk that has been preserved by freezing and liquefied before feeding does not differ from fresh milk in total solids, fat, carbohydrates or protein. The bacterial counts were surprisingly low. The vitamin content of fresh human milk was not changed by the process of freezing. Nine premature babies who were fed on the milk gained as satisfactorily as they would have on fresh milk. Recently sixteen premature babies have been observed, making a total series of twenty-five infants who have been fed on the so-called frozen milk. The oldest baby was one-half month premature; the youngest, three months premature. Eight were boys, and seventeen, girls. The weight at birth averaged 3.1 pounds (1,406 Gm.); the largest baby weighed 4 pounds and 13 ounces (2,182 Gm.) and the smallest baby weighed less than 2 pounds (less than 907 Gm.). The patients varied in length from 14 to 20 inches (35.56 to 50.8 cm.), the average length being 17 inches (43.18 cm.). In most cases, the body temperature became stabilized at the age of 3 weeks. During the period of observation nine babies showed clinical signs of atelectasis; three had otitis media; two, mycotic stomatitis; three, a dermatitis; one, an infected finger; one, an umbilical abscess; one, conjunctivitis, and one, a birth injury and hydrocephalus. One baby was gravely ill with frequent attacks of cyanosis for the first few days. One other baby who had advanced syphilis was critically ill on entry.

The age of the frozen milk varied from one to two hundred and twenty days and it was fed to the infants over periods ranging from four to ninety-nine days, the average being thirty-four days. The bacterial counts were very low, twenty colonies per cubic centimeters, for example, in frozen milk examined five months later.

The average age at which orange juice and cod liver oil (or viosterol) were added to the babies' milk was 4.1 weeks, the youngest baby being 2.5 weeks old

when they were added and the oldest nine weeks. Antirachitic and antiscorbutic vitamins were added at about the same time whether the infants were being fed fresh or frozen milk.

The series may be divided into three groups: (1) infants who received fresh human milk, (2) infants who received frozen human milk and (3) infants selected from groups 1 and 2 who received fresh human milk for one period and frozen milk for another. If the weight gained by the babies on fresh milk is compared with that gained by the babies on frozen milk, it will be seen that, as among the three groups, the difference would amount to less than 6 ounces (170.09 Gm.) a month. If the babies are taken by pairs (twins), the gain of those on frozen milk differs very little from the gain of those on fresh milk.

GENGENBACH, Denver.

VITAMIN D MILK IN THE TREATMENT OF INFANTILE RICKETS. BENJAMIN KRAMER and ISAAC F. GITTLEMAN, New England J. Med. **209**: 906 (Nov. 2) 1933.

Ten children, aged from 3 to 22 months (three white and seven colored), suffering from rickets were treated with vitamin D milk, produced either by irradiating the milk directly with ultraviolet rays from a carbon arc lamp or by feeding irradiated yeast to the lactating cattle. The ten infants were divided into four groups, making it possible to feed each type of milk at two levels of vitamin D, that is, 55 and 40 Steenbock units respectively per child daily. In each group healing began in from seven to thirty-one days, the average period being about two weeks. Healing was well advanced in from four to six weeks. The calcium and inorganic phosphorus of the serum followed the same course as during treatment with cod liver oil. Infants showing low calcium or low phosphorus or a decrease in both elements in the serum responded equally well to both types of vitamin D milk whether these were fed at the high or at the low level of vitamin D. Aside from gastro-intestinal disturbances resulting from accidental infection, the milk was well tolerated by all the children.

The effectiveness of treatment was determined by noting the interval between the beginning of treatment and the appearance of the first roentgenographic signs of healing; also when healing appeared to be well advanced or complete. In every instance the chemical findings in the blood serum indicated active rickets, and improvement in these ran parallel with the roentgenographic appearance of new calcium deposition. When healing was well advanced, as seen by roentgenograms, the Ca×P product was well outside the rachitic zone. All the patients had one or more clinical signs of rickets. Invariably the children became more active and were obviously better subjectively. Craniotabes disappeared, but one or more of the other clinical signs persisted.

The authors conclude that: 1. The definite curative action of as little as 40 Steenbock units daily shows vitamin D milk to be the most effective of antirachitic agents. 2. At the levels fed there was no significant difference in effectiveness between vitamin D milk prepared by direct irradiation and vitamin D milk produced naturally by feeding cows irradiated yeast. 3. The apparent discrepancy between the minimal clinically effective dose of vitamin D in the form of vitamin D milk and that of this vitamin in the form of cod liver oil or viosterol requires further investigation.

GENGENBACH, Denver.

PLASMA PHOSPHATASE IN RICKETS AND OTHER DISORDERS OF GROWTH. JEAN SMITH, Arch. Dis. Childhood **8**:215 (June) 1933.

The average plasma phosphatase of ten normal breast-fed healthy infants was found to be 0.248 units, with a range of from 0.2 to 0.3 units. The plasma phosphatase of a group of healthy infants fed on artificial foods and given additionally fat-soluble vitamins A and D and water-soluble C, ranged from 0.2 to 0.36 units, with a mean value of 0.3 units, i. e., approximately the same as that of healthy

breast-fed infants. The plasma phosphatase is increased in active rickets. In sixteen cases of roentgenologically diagnosed rickets it varied from 0.41 to 1.29 units with an average of 0.772 units. In a series of infants fed on artificial foods, but not receiving extra fat-soluble vitamins, the average plasma phosphatase was 0.52 units with a range of from 0.4 to 0.702 units. As long as these vitamins were withheld the plasma phosphatase increased and when these were added the values fell to within normal limits. The plasma phosphatase is increased in active rickets and returns to normal with antirachitic treatment. The serum calcium and phosphorus are not true criteria of the presence or absence of rickets unless the rate of growth is also taken into account. Plasma phosphatase is perhaps a much more sensitive index of abnormal metabolism of the bones in rickets.

KELLY, Milwaukee.

CERTAIN OBSERVATIONS IN CLINICAL AND EXPERIMENTAL STUDY ON THE ETIOLOGY AND TREATMENT OF RICKETS. B. B. BHATTACHARYYA, Calcutta M. J. **27**:372 (April); 405 (May) 1933.

PART I.—The author believes that a deficiency of vitamin D is not as important in the causation of rickets as is a lack of "specificity" of breast milk, and that this "specificity" becomes lost in maternal exhaustion or devitalization from repeated pregnancy or prolonged nursing. Guinea-pigs 2 months of age fed on breast milk from women having at least seven children showed evidence of osteoporosis (first stage of rickets) in twenty-five days. This is proof that human milk from devitalized mothers has a poisonous effect on the osteoblastic activity of the growing bones. Vitamin D certainly has a curative and prophylactic influence in rickets, but that alone does not mean that a deficiency of the same vitamin is the cause of the disease.

The author has observed 280 cases of rickets during the past four years in his practice in India. The incidence of rickets is on the increase in India because of the gradual disappearance from the urban centers of the time-honored customs of regularly exposing the baby to the sun after the fifth day and of regularly exposing the mother's body, especially the breasts, to the sun.

PART II.—Viosterol is a powerful and specific therapeutic agent in the treatment of rickets. In India it is efficacious in smaller dosage than that prescribed by the manufacturers. This is presumably due to the milder forms of rickets found in India and to the presence of abundant available ultraviolet rays from the sun.

GONCE, Madison, Wis.

A CASE OF GASTRIC RETENTION. JEAN LEVESQUE and SUZANNE DREYFUS, Bull. Soc. de pédiat. de Paris **30**:172 (March 15) 1932.

A boy, 4 months old, vomited a great deal and did not thrive. Four hours after feeding there was still some food in the stomach, as evidenced on the passage of a stomach tube. The contents of the stomach showed a high acidity but no free hydrochloric acid. Roentgenologic examination revealed no pyloric obstruction, spasm or prepyloric dilatation, and there was no evidence of hypomotility. A number of infants who showed a similar clinical picture, in which vomiting and failure to gain weight were the predominating symptoms, also had some gastric retention but no evidence of mechanical obstruction. It is believed that such infants have a congenital intolerance for certain foods, notably milk of high fat content and sweetened condensed milk, and that if fed skim-milk or buttermilk they will stop vomiting.

BENJAMIN, Montreal, Canada.

SOY BEAN MILK IN THE FEEDING OF INFANTS. MARCEL MAILLET, L. YEU and K. YEU, Bull. Soc. de pédiat. de Paris **30**:488 (Oct. 18) 1932.

The authors make a milk from soy beans; they were ground up under a stream of water and the resultant mixture was strained. Sugar, cream of rice, calcium

carbonate and sodium chloride were added to the milk and it was fed to 100 infants. Each feeding had a fuel value of 700 calories per liter. The food was comparatively well tolerated by all the infants, even by those who had evidence of indigestion just before the soy milk feeding was begun. The authors conclude that this vegetable milk has a limited field of use for infants who have an intolerance for cow's milk and that it is to be used in those cases for only a temporary period.

BENJAMIN, Montreal, Canada.

UVIOSENSITIVE DYSTROPHIES IN OLDER CHILDREN AND ADOLESCENTS. GEORGES SCHREIBER, Bull. Soc. de pédiat. de Paris **30**:507 (Oct. 18) 1932.

Ultraviolet irradiation was administered to two boys and five girls who were markedly underdeveloped and undernourished. This was followed by increases in weight of from 1 to more than 3 Kg. in six weeks. There was evidence of some endocrine disturbances, and it is suggested that the vegetative nervous system was acted on by the actinic rays to produce the favorable results.

BENJAMIN, Montreal, Canada.

PHYSIOLOGIC AND THERAPEUTIC DIFFERENCES BETWEEN IRRADIATED STEROLS AND ULTRAVIOLET RAYS. P. DUHEM and E. HUANT, Presse méd. **41**:1472 (Sept. 23) 1933.

Experiments to determine the relative effects of ultraviolet irradiation and irradiated sterols on the vegetative nervous system were conducted by Duhem and Huant, using as their standards three reactions: the oculocardiac reflex, the cardiac response to atropine and the cardiac response to epinephrine. A number of children from 5 to 13 years of age were tested. Following ultraviolet irradiation variations of from 12 to 22 in the cardiac rate occurred, as compared with the usual response to the stimuli named, while average doses of the irradiated sterols produced changes ranging from 0 to 2. The authors conclude that the effect of the irradiated sterols on the vegetative nervous system is very slight, as compared with the marked effect of ultraviolet irradiation.

BIEKER, St. Petersburg, Fla.

VARIATIONS OF CALCIUM CONTENT IN THE BLOOD SERUM AS INFLUENCED BY VIOSTEROL AND ULTRAVIOLET IRRADIATION. G. CAREDDU and R. CENTO, Pediatria **41**: 1349 (Nov.) 1933.

In twenty-six normal children between the ages of 1 and 9 years there was a constant and steady increase of the calcium content of the blood with the use of ultraviolet rays and viosterol, the increase being especially marked in children in whom the calcium content was originally below 10 mg. per hundred cubic centimeters (this being assumed as normal). With therapeutic doses the increase reached a maximum of 12 mg. per hundred cubic centimeters, and only rarely did it go higher. The maximum was reached after from twenty to twenty-five days of treatment, after which the calcium content remained stationary or tended to decrease.

SIGNORELLI, New Orleans.

A REGIMEN OF TRANSITION TO VEGETABLE PROTEIN IN THE TREATMENT OF INFANTILE DIARRHEAS. CAHARE, Bull. Soc. de pédiat. de Iasi **3**:115 (Oct. 31) 1932.

Cahare believes that it is advisable to offer protein as well as carbohydrate food to infants with diarrhea immediately after the starvation period before the ordinary diet can safely be resumed. Vegetable protein, as furnished by soy bean, is considered superior to animal protein for the infants' tolerance and digestiblity. Excellent results were obtained by feeding a bouillon of the follow-

ing composition: cream of rice, 10 parts, soy bean cereal, 4 parts, sugar, 5 parts, extract of malt, 2¼ parts, and water, 80 parts. One liter of this bouillon contains 720 calories.

LEMASTER, Evanston, Ill.

VITAMIN C IN COW'S MILK. HANNA SZLENDAKOWA, Pedjatrja polska **12**:471, 1932.

After an extensive investigation on guinea-pigs, the author concludes that the amount of vitamin C in cow's milk depends on whether the milk is obtained in the summer or in the winter. Thirty cubic centimeters of raw milk given to a guinea-pig which weighs 350 Gm. and is maintained on a synthetic diet does not keep the animal alive. From 60 to 75 cc. of raw milk obtained in the winter does not protect a guinea-pig from scurvy. From 60 to 75 cc. of raw milk obtained in the spring protects a guinea-pig from scurvy only partially. It is safe to conclude that the source of vitamin C in cow's milk is not present in sufficient quantity to prevent scurvy.

KRUPINSKI, Chicago.

SOY BEANS IN THE INFANT'S NUTRITION. METABOLISM EXPERIMENTS ON SIX INFANTS. G. KRAUSE and M. T. LASSEN, Arch. f. Kinderh. **100**:226 (Oct.) 1933.

Six infants on whom metabolism tests were being made gained weight and showed a positive nitrogen balance when fed a soy bean preparation. However, the absorption and retention of nitrogen was not as great during this period as during the control periods when buttermilk was fed. Confirming the work of others, the authors found that soy bean flour tends to shift the acid-base equilibrium of the body toward the alkaline side.

LEMASTER, Evanston, Ill.

RÔLE OF MASTOIDITIS IN TOXICOSIS OF INFANCY. EDE VON GYÖRGY, Arch. f. Kinderh. **100**:238 (Oct. 31) 1933.

Twenty-seven cases of antrotomy in infancy are reported. In three cases there was uncomplicated mastoiditis, and in twenty-four cases, latent mastoiditis associated with symptoms of intoxication. The mortality in the latter group was 55 per cent. In some cases the infection of the antrum began at the onset of the intoxication, in other cases during the course of the intoxication and in still other cases during convalescence from the intoxication. In every case the antrum was found to be inflamed and edematous or to contain frank pus. Recovery from antrotomy was usually complete within from five to eight weeks. György believes that bilateral antrotomy is indicated when the cause of intoxication is not apparent, even though examination of the ear does not show definite signs of mastoiditis.

LEMASTER, Evanston, Ill.

URINARY PROTEIN. S. KOZAWA, R. IWATSURU and T. ADACHI, Biochem. Ztschr. **260**:313, 1933.

Fresh urine, containing protein, is filtered and decolorized with animal charcoal. The protein is precipitated with 20 per cent sulphosalicylic acid and washed with water. At a definite salt concentration this urinary protein has an iso-electric point at p_H 4.4, which corresponds well with that for serum protein. On hydrolysis it yields from 80 to 82 per cent α-amino acids, from 1.04 to 1.29 per cent histidine, from 0.86 to 1.12 per cent tryptophan and from 4.56 to 4.98 per cent tyrosine, which likewise resembles the composition of the serum proteins. The ratio of albumin to globulin is also that of the serum proteins, so that all evidence tends to show the direct derivation of the urinary protein from the serum protein.

KUGELMASS, New York.

INFLUENCE OF EXTRACT OF THE ANTERIOR LOBE OF THE PITUITARY GLAND AND THYROTROPIC SUBSTANCE ON THE GASEOUS METABOLISM. OTTO L. DIFFENBACH, Endokrinologie **12**:250, 1933.

Neither the injection of extract of the anterior lobe of the pituitary gland into infantile female rats nor injections of the urine of pregnant women into adult male guinea-pigs has any influence on the gaseous metabolism. On the contrary, injection of the thyrotropic substance causes an increase in the metabolism of adult rats and guinea-pigs which varies with the amount injected. In the rat the effect of the injection manifests itself after one and a half hours and disappears in twenty-four hours; in the guinea-pig the effect appears in twenty-four hours and begins to disappear slowly after forty-eight hours. However, in thyroidectomized animals the thyrotropic substance no longer exercises a stimulating action on the metabolism, which falls below normal.

KUGELMASS, New York.

ACTION OF THE APPLE DIET. GÜNTHER MALYOTH, Klin. Wchnschr. **10**:1159 (June 20) 1931.

The favorable results of the Heisler-Moro apple diet in the treatment of diarrhea are ascribed by Moro to the effect of the tannic acid content in the apple, but the tannic acid strength is only 0.068 per cent. Heisler attributes the good results to the specific acid effect of the fruit by which an alteration of the intestinal flora may be produced, but the malic acid content is only 0.59 per cent. The author believes that the effect may be due to the pectin content and the physicochemical properties of this substance. Its colloidal nature provides the large surface which must be of importance in the adsorption of toxic substances. Then the action of pectin as a buffer substance must be considered, and the further chemical actions which may arise from the formation of galactronic acid as well as from the separation of calcium and magnesium salts in consequence of the hydrolysis of pectin. He concludes by pointing to the numerous possibilities and problems involved in the action of the apple diet in diarrhea.

SILVERMAN, Syracuse, N. Y.

COMPARISON OF RAW APPLE WITH APPLE POWDER IN THE TREATMENT OF DIARRHEA. GÜNTHER MALYOTH, Klin. Wchnschr. **10**:1255 (July 4) 1931.

The acid content of fresh apple juice as well as of apple powder was found to vary from p_H 3.3 to 3.75, depending on the kind of apple and the degree of ripeness. The pectin content was found to be twice as high in the powder as in the fresh apple. The author thinks that this provides evidence that the pectin content is the important element, since proportionately less of the powder was required to improve diarrheal conditions.

SILVERMAN, Syracuse, N. Y.

APPLE POWDER IN THE TREATMENT OF DIARRHEA IN CHILDREN. ALFRED WISKOTT, Klin. Wchnschr. **10**:1252 (July 4) 1931.

The author reports that the usual raw apple diet (apples peeled, cored and grated) was not effective in treating bacillary intestinal diarrhea. The presence of blood in the stools and the tenesmus were not affected readily. He believes that the preparation of the apple diet in the home is not always reliable and that the diet does not look sufficiently attractive to the patient. An apple powder, which provides less residue and finer division, makes the stools look more homogeneous, fine-grained and less watery. Rapid improvement was observed in more than thirty cases that had been stationary. On the first day, from 20 to 24 Gm. was given and on the second day from 30 to 40 Gm. A 4 per cent suspension was used at first, which was increased to 8 per cent the next day (10 per cent would correspond to the grated fresh apple).

SILVERMAN, Syracuse, N. Y.

PHYSICOCHEMICAL AND CLINICAL STUDIES OF CHOLESTEROL METABOLISM. W. SCHEMENSKY and J. MRUGOWSKY, Ztschr. f. d. ges. exper. Med. **85**:329, 1932.

There is little correlation between serum cholesterol and rise of blood pressure; any that exists is to be attributed to the greater age of the patients with hyperpiesia. With increasing age there is a rise in the average serum cholesterol. Of twenty patients with arteriosclerosis the serum cholesterol was raised in eleven; the rise is attributed to the relative impermeability of the vessels through which it leaves the blood. Residence at high altitude produced an increase, possibly the result of splenic action. In infectious diseases there is a fall in cholesterol at the height of the infection and a rise during convalescence. The initial fall is attributed to the fixing of the cholesterol by toxins. In diabetes the level of the cholesterol is related in great part, but not entirely, to general fat metabolism. In nephritis there is no correlation between cholesterol and blood pressure or the ability to excrete water or concentrated solids. In patients with neoplasms the level of cholesterol varies, and it is suggested that the rate of growth of the tumor is the deciding factor.

KUGELMASS, New York.

FURTHER INVESTIGATIONS ON THE BREAKDOWN OF AMINO-ACIDS IN THE ANIMAL BODY. HANS A. KREBS, Ztschr. f. physiol. Chem. **218**:157, 1933.

The identification of a-keto-acids as intermediate products in the oxidative deamination of alpha-amino-acids by renal tissue has been successful in a number of instances, but not with the dibasic asparaginic and glutamic acids. The latter underwent further breakdown. By poisoning the tissue cells with 0.001 mg. arsenic trioxide, the reaction can be stopped at the keto-acid stage, so that asparaginic and glutamic acids yield the same type of products as the monobasic amino-acids. Glutamic acid gave a-hetoglutaric acid, isolated as the 2, 4, *di*-nitrophenylhydrazone, m. 222°. Asparaginic acid gave oxalacetic acid, demonstrated by the $PhNH_2$ reaction, and pyruvic acid, isolated as the 2, 4, *di*-nitrophenylhydrazone, m. 216°. The $HO_2CCOH_2CO_2H$ rapidly loses carbon monoxide even in the absence of an enzyme, so that the main product is $AcCO_2H$. The arsenic trioxide arrests not only the further breakdown of keto-acid, but also the reactions involving the NH liberated so that the latter accumulates in greater amounts.

KUGELMASS, New York.

CONTENT OF ANTIRACHITIC VITAMIN IN COW'S MILK AND HUMAN MILK. J. VAN NIEKERK, Maandschr. v. kindergeneesk. **2**:525 (Aug.) 1933.

The antirachitic activity of milk was studied in rats made rachitic, and the result was compared with the activity of the international standard for vitamin D. As it was practically impossible to give enough milk to each animal daily to make an improvement in the rachitic bones probable only the fat of the milk was investigated. Van Niekerk found that cow's milk does not provide vitamin D in amounts sufficient for the child. In confirmation of the results obtained by Hess, Steenbock and other investigators he found further that the milk of cows which have received extra amounts of vitamin D is still too poor in that vitamin.

The amount of antirachitic vitamin in the human milk investigated was nearly equal to that in cow's milk.

VAN CREVELD, Amsterdam, the Netherlands.

Prenatal Conditions

CONGENITAL ANOMALY OF THE HEART WITH TRANSPOSITION OF THE AORTA. L. KETTLER, Virchows Arch. f. path. Anat. **287**:10, 1932.

The heart, which is described in detail, came from a child who died at the age of 15 months. The clinical diagnosis during life had been congenital cardiac

anomaly, with a surmise of defective ventricular septum and open ductus arteriosus. The auricular and ventricular septums were defective. There were three ventricular cavities. The third ventricle, which gave rise to a pulmonary artery with only two valve segments, had been formed by division of the right ventricle by the persistent septum of the bulbus arteriosus. There was no right auriculoventricular orifice; the left had five valve segments. The aorta arose from the right ventricle; the coronary arteries were transposed. The left superior vena cava was persistent; the right had disappeared. The pulmonary veins entered the heart by a single trunk. There was a persistent coronary sinus with two valves.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

UNUSUAL ANOMALY OF THE FACE IN AN ANENCEPHALIC MONSTER. B. RATING, Virchows Arch. f. path. Anat. **288**:223, 1933.

In an anencephalic monster, 32 cm. in length, an accessory nose was situated between a double right eye and the root of the normal median nose. The upper lip, palate and maxilla were cleft. The maldevelopment is made the basis of a discussion of incomplete reduplication anomalies of the face.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

CONGENITAL ATRESIA OF THE LARYNX WITH HYPERTROPHY OF THE LUNGS AND GENERALIZED HYDROPS. A. KOVÁCS, Virchows Arch. f. path. Anat. **288**: 243, 1933.

In a female infant weighing 2,500 Gm., respiratory movements and contractions of the heart continued for twenty minutes after birth. The body was markedly edematous, and the peritoneal cavity was filled with fluid. Necropsy revealed complete atresia of the larynx and marked enlargement of the lungs. Other anomalies were absence of one kidney, ovary and oviduct; atresia of the anus and vagina and ankyloblepharon. The increase in the size of the lungs was due to distention of the alveoli by mucus. The pulmonary hypertrophy and the hydrops were the direct results of the atresia of the larynx, which interfered with the escape of mucus from the bronchial system. Hydrops was the result of mechanical compression of the heart and vessels by the distended lungs. According to the author, only seven samples of congenital atresia of the larynx have been previously reported. In one of these the lungs were enlarged and there was hydrops. In other cases the state of the lungs was not noted. The author thinks that the enlargement was overlooked, since hydrops was present in several cases.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

ACCESSORY TONGUE. K. M. MENZEL, Virchows Arch. f. path. Anat. **288**:253, 1933.

Anomalies previously described as accessory tongue have been rounded masses in the floor of the mouth that contained cartilage or adipose tissue and that were attached to the body of the hyoid bone or to the septum of the tongue. They have had little structural resemblance to the normal tongue. Menzel carefully describes as accessory tongue two examples of a congenital anomaly that he claims has never been heretofore recorded. One was in a youth, aged 16, the other in a woman, aged 26. In each instance the accessory tongue was about the size of a walnut. It exhibited spontaneous fibrillary and coarser contractions and had a papillary surface like that of the base of the tongue. In the boy the mass was attached to the lower pole of the left tonsil. In the woman it was attached to the right side of the base of the tongue; the right tonsil and faucial pillars were absent. In each case the anomaly was associated with atresia of the external auditory canal, absence or maldevelopment of the external ear, maldevelopment of the middle ear and congenital paresis of the facial nerve, in

each case on the same side as the lingual anomaly. The internal ear and labyrinth were functionally normal. Taste sensation of the accessory tongue of the boy was carefully tested and was found to be present and normal. Histologic examination of the structure after removal showed it to have a surface like that of the normal tongue, with filiform and circumvallate papillae and taste buds. The deeper portion of the mass consisted of striped muscle. Atresia auris associated with paresis of the facial nerve has frequently been described. These conditions are ascribed to defective development arising not later than the third fetal month in the region of the first and second branchial arches. Menzel believes that the accessory tongue described by him arose from multipotent tissue of this same region.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

PARTIAL CONGENITAL ABSENCE OF THE PANCREAS. CHRISTLIEB, Virchows Arch. f. path. Anat. **289**:241, 1933.

The author adds one to the small number of reported cases of congenital partial absence of the pancreas. The patient was a woman who died at the age of 69 of cerebral hemorrhage. On the day before death the urine contained a trace of sugar. Sugar had not been present when she was under treatment for pneumonia a year and a half before death. The pancreas measured 8 by 4 by 1.5 cm. and was closely attached in the concavity of the duodenum. It consisted of a small head, an uncinate process and a small part of the body. Histologically, the islets were numerous and large, a condition interpreted as compensatory. The anomaly is ascribed to failure of development of the dorsal anlage of the pancreas.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

CASE OF SYNDACTYLISM AND GIGANTONYCHIA. E. SIGAL, Časop. lék. česk. **71**: 329 (March 11) 1932.

The author presents the case of a girl, aged 14 years, with a right hand on which there were two single phalanx fingers. One was the fifth finger; the other, with a nail 4 cm. wide, replaced the remaining three fingers and the thumb. Roentgen pictures revealed absence of the third and fourth metacarpal bones and their phalanges. The first and second metacarpal bones were fused and prolonged, and the fifth was likewise prolonged, and both digits were hooked and turned inward. By means of plastic surgery, the sulcus between these two digits was deepened so that the result was an extremity which was useful for writing and holding objects.

STULIK, Chicago.

DERMATOGLYPHS OF THE PALMS AND SOLES AND THEIR RELATION TO THE BONES IN HIGH GRADE SYNDACTYLISM. J. A. VALSIK, Časop. lék. česk. **71**: 354 (March 18) 1932.

The epidermal configurations on the palms and soles of three patients with high grade syndactylism were studied in relation to the bones of the hands and feet. The preparations of an adult and two new-born infants were preserved in alcohol so that the corneum had to be removed for the study of the skin. Small pins were placed in the triradius, roentgenograms were taken, and, with the aid of magnifying glasses, drawings were made. A striking diminution of the palmar and plantar triradii was evident (oligodactylism), and from the roentgenogram in one case a more or less distal dislocation of the triradii in relation to the bones could be noted. Why the oligodactylia and distal dislocation of epidermal configuration appear is difficult to explain. Bonnevie entertained the belief that epidermal configurations are related to the cutaneous nerves, and that perhaps the cutaneous configurations as well as the syndactylism are caused by a disturbance in innervation. This work is dedicated to Dr. Matiegka, professor of anthropology at Charles University, on the advent of his seventieth birthday.

STULIK, Chicago.

CONGENITAL OSTEOPOIKILOSIS. VACLAV SVAB, Časop. lék. česk. **71**:742 (June 10) 1932.

On routine examination roentgenograms revealed typical areas of condensation in the wrists of a man 26 years of age. His brother, 28 years of age, and the father, aged 54, were found to have the same condition, except that the sons had an involvement of all the bones except the skull. In the father the condensations were present chiefly in the extremities. The father had, in addition, dermatofibrosis lenticularis disseminata. The finding of this condition in father and sons points to the alinement of the trabeculae of the spongiosa into the condensed areas as a hereditary tendency along with diabetes, which was also present.

STULIK, Chicago.

Diseases of the New-Born

ERYTHROLEUCOBLASTOSIS IN THE NEW-BORN. R. C. WANSTROM, Am. J. Path. **9**:623, 1933.

A case of fetal erythroleukoblastosis with ascites is reported, in which microscopic study revealed certain unusual features. In addition to marked hematopoiesis in the liver, spleen, kidney, bone marrow, lymph nodes, thymus, diaphragm, pharynx, small intestine and pancreas, similar foci were present in the chorionic villi. In the lesser bile ducts and in some renal tubules numerous giant cells were observed, apparently resulting from alterative changes in damaged epithelium. The generic relationship and probable intrinsic constitutional etiology of congenital hydrops, icterus gravis and fetal erythroleukoblastosis of the new-born are pointed out, and suggestions are made as to future investigation along these lines.

AUTHOR'S SUMMARY. [ARCH. PATH.]

ENLARGED THYMUS AND ATELECTASIS IN THE NEW-BORN. HYMAN GOLDSTEIN, Arch. Pediat. **50**:578 (Aug.) 1933.

The author reports a case.

WADDELL JR., University, Va.

EXPERIMENTAL CUTANEOUS INDURATIONS IN THE NEW-BORN. HORIA SLOBOZIANO, MARIUS GEORGESCO and P. HERSCOVICI, Bull. Soc. de pédiat. de Paris **30**:165 (March 15) 1932.

One hundred and four infants born at term were studied in the first forty-eight hours of life. In fifty-five the skin was traumatized by pinching or stroking. In 39 per cent of the cases it showed slight induration, and in 3.6 per cent it showed hard plaques. Of a series of twenty-four infants who were subjected to freezing of the skin by means of a spray of ethyl chloride, 70.8 per cent had local reactions; 72 per cent of a series of twenty-five infants who were subjected to freezing and trauma of the skin presented similar reactions. Two biopsies, one of skin which had been frozen and another of skin which had been both frozen and traumatized, showed atrophy of the subcutaneous adipose tissue cells, with thickening of the areolar connective tissue cell structure. This histologic picture is similar to that found in the cutaneous indurations of the new-born. Whereas in some instances trauma to the skin may have occurred during birth, in others there was no evidence of this. It is thought that in some cases postnatal chilling of the skin may be a factor in the production of areas of induration of the skin.

BENJAMIN, Montreal, Canada.

GASEOUS PYOCOLPOS DUE TO COLON BACILLUS IN A NEW-BORN INFANT. H. L. ROCHER and BALARD, Bull. Soc. de pédiat. de Paris **30**:208 (March 15) 1932.

A new-born girl, weighing 3,100 Gm., seemed perfectly normal after a spontaneous delivery. Two days later, some swelling of the labia majora was noticed.

This increased, and the entire vulva and perineum became markedly swollen, although the skin and subcutaneous tissues were not inflamed. The hymen was imperforate. Rectal examination revealed a bulging of the posterior wall of the vagina into the rectum. When the infant was 11 days old, a syringe was inserted into the swelling, and considerable foul-smelling gas and a small quantity of pus were aspirated. The pus showed numerous colonies of colon bacilli, a few short chains of streptococci and epithelial cells. Incision of the hymen was performed, and the abscess was drained. This had to be done a second time a few days later, as the opening in the hymen had closed. The condition gradually improved. When the child was seen at 18 months of age, she had a normal falciform hymen.

BENJAMIN, Montreal, Canada.

TRANSOSSEOUS VASCULAR ANASTOMOSIS BETWEEN THE MAXILLARY SINUS AND THE ORBIT IN THE HUMAN FETUS AND IN THE NEW-BORN. H. RICHTER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **137**:89 (Nov. 24) 1933.

Richter studied serial sections of the nose (frontal sections) of human fetuses and new-born infants to verify the existence of transosseous vascular anastomoses between the maxillary sinus and the orbit. At the end of the fourth fetal month the space between the maxillary sinus and the cartilaginous nasal capsule which divides the sinus from the orbit is filled with connective tissue. The bone is in a state of active transformation. In some osseous spaces filled with connective tissue the mesenchyma was observed to contain blood vessels. These constitute the anlage for the later transosseous anastomoses. In the eighth month, at which time the bone constitutes the sole and permanent wall between the sinus and the orbit, the marrow spaces contain numerous blood vessels. Connections between these and the vessels in the lining of the orbit and the maxillary sinus were demonstrable in many places. In one section, in spots where the bone was especially thin, transosseous vessels could be traced from the sinus into the orbit. The author suggests that these transosseous vascular paths may play a rôle in the spread of infection from the maxillary sinus to the orbit in later life.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

RÔLE OF THE PREMATURE INFANT IN THE PRODUCTION OF A HIGH MORTALITY OF THE NEW-BORN. J. SZÉNÁSY, Gesundhfürs. f. d. Kindesalt. **8**:198 (Aug.) 1933.

The statistics collected in Hungary demonstrate that premature birth is at present the most important cause of mortality among the new-born.

REICHLE, Cleveland.

STUDY OF ICTERUS IN THE NEW-BORN. H. FUJIMORI, Jap. J. Obst. & Gynec. **16**:258 (June) 1933.

Fujimori presents his investigation of the relation between the changes in the quantity of bilirubin in the serum of the new-born, the destruction of erythrocytes and the behavior of the hematogenic organs. These researches were carried out on blood obtained from the superficial temporal vein; the bilirubin was detected and measured by the Saeki method. He concludes that bilirubinemia is present at the time of birth, and that it increases to an average of 38.16 units on the sixth day and then gradually decreases until it disappears on the seventeenth day after birth. When the quantity of bilirubin reaches 16.3 units jaundice reveals itself in the skin. At the same time the blood shows an increase of the red cells to twice the normal number within two hours after birth and then a decline to the lowest level on the seventh to the tenth day after birth. But while the destruction of the red cells goes on, the nucleated red cells, which decrease in number after birth, show a tendency to increase again as soon as the bilirubinemia becomes marked, which suggests the activity of the hematogenic organs. Since Verza and

Zih have advocated that bilirubin be called the "hematopoietic" hormone, Fujimori thinks that if their conception is true, the bilirubin produced by the destruction of erythrocytes in icterus neonatorum is being used either to stimulate the hematogenic organs to greater production of red cells or to prevent the destruction of other erythrocytes.

ADAIR, Chicago.

Acute Infections

DIPHTHERIA IMMUNIZATIONS AND ANAPHYLAXIS. ARTHUR S. SANDLER, Arch. Pediat. **50**:512 (July) 1933.

Nothing new is presented, and for this reason the article is not abstracted.

WADDELL JR., University, Va.

DIPHTHERIA CONTROL IN CHICAGO. H. N. BUNDESEN, W. I. FISHBEIN and H. C. NIBLACK, J. A. M. A. **100**:1093 (April 8) 1933.

The mortality from diphtheria in Chicago has been materially reduced by personal solicitation by nurses of permission for inoculations beginning at the age of 6 months. An addressograph list of names of all children under 1 year of age, maintained up to date, has been a great aid in the campaign for the prevention of diphtheria. With the use of alum-precipitated toxoid, reactions are fewer, immunity develops more rapidly, and a greater number become immune with two inoculations. In communities where there are many foreign-born the church has been invaluable in promoting public health work. Literature alone is not very valuable in bringing about immunization, but it paves the way for the visits of nurses.

BONAR, Salt Lake City.

DIPHTHERIA IMMUNIZATION WITH A SINGLE INJECTION OF PRECIPITATED TOXOID. A. H. GRAHAM, L. R. MURPHEE and D. G. GILL, J. A. M. A. **100**:1096 (April 8) 1933.

A single injection of from 5 to 10 units of precipitated toxoid changed the reaction to the Shick test from strongly positive to negative in 171, or 92.4 per cent, of 185 children. The results indicate that a single injection of the toxoid precipitated with alum results in immunity in a high percentage of cases. It is as effective as two or three injections of the best unprecipitated toxoid.

BONAR, Salt Lake City.

AMIDOPYRINE IN THE TREATMENT OF MEASLES. M. P. BOROVSKY and F. STEIGMANN, J. A. M. A. **100**:1859 (June 10) 1933.

The reports of the specificity of amidopyrine in the treatment of measles in the past few years is not borne out in studies of 194 patients with measles. The drug was found to be a valuable antipyretic, but it did not prevent the eruption of measles, lessen the complications or shorten the course of the disease.

BONAR, Salt Lake City.

ORORHINOLOGIC ASPECT OF SCARLET FEVER WITH PARTICULAR REFERENCE TO THE SINUSES. G. D. HOOPLE and L. S. CANE, J. A. M. A. **101**:1121 (Oct. 7) 1933.

A series of 292 patients with scarlet fever were studied clinically and roentgenographically for sinusitis. Roentgenographic evidence was found in 90 per cent, but clinical evidence was not present in this percentage. Among the 292 patients of this group there were 33 who had otitis media and there were 12 more in a second series of 80 patients. In all these there was roentgenographic evidence

of sinusitis. In all but one the involvement was on the side of the infected ear. The question is raised as to whether or not involvement of the sinus is the rule rather than a complication.

BONAR, Salt Lake City.

SERUM TREATMENT OF MENINGITIS. JOSEPHINE B. NEAL, New York State J. Med. **33**:94 (Jan. 15) 1933.

In the past twenty-two years the division on meningitis of the New York City health bureau has observed 1,100 cases of meningococcic meningitis. All patients with purulent meningitis are given antimeningococcic serum unless some other organism is shown. In the treatment of epidemic meningitis serum is given intraspinally every twenty-four hours until two successive specimens of spinal fluid are negative on smear or culture. The subarachnoid space is thoroughly drained; the amount of fluid removed governs the amount of serum administered. Intramuscular or intravenous injections are used only in meningococcic septicemia. It is rarely safe to give less than four doses of serum. The cell count is not of great value as an indication of when to stop treatment, since cell counts on different portions of spinal fluid show variation and since the prognosis is bad if the cells disappear and the organisms persist. While cisternal and ventricular punctures may be necessary if blocking occurs, they should be avoided if possible because of the greater danger of injury.

When results are not obtained with one serum, change should be made to another product. Unsatisfactory results may be due to overtreatment; an injection is rarely necessary more than once in twenty-four hours. In a few patients reacting unfavorably to serum autogenous vaccines have been given subcutaneously or intraspinally.

Of 302 patients treated in the past five years, 57 have died (18.3 per cent). Of the 57 patients, 7 received only one injection of serum. No patients with pneumococcic meningitis have recovered, but the appropriate type of serum is still used. Six of 164 patients with streptococcic meningitis recovered. Of 90 patients with influenzal meningitis, 3 have recovered.

AIKMAN, Rochester, N. Y.

THE USE OF CONVALESCENT SERUM IN THE TREATMENT OF MEASLES, CHICKENPOX, MUMPS AND WHOOPING COUGH, INCLUDING THE PROPHYLACTIC VALUE OF PARENTAL BLOOD. J. M. LEWIS and L. H. BARENBERG, New York State J. Med. **33**:97 (Jan. 15) 1933.

Fifty-six children exposed to measles were given intramuscular injections of whole blood. Sixty-four children were given convalescent serum from patients who had recently recovered. Twenty-three patients were untreated, and frank measles developed in all of them, while 23 per cent of the fifty-six children remained free from measles. Sixty-four per cent were definitely benefited by injections of adult whole blood. It must be given during the first five days of the period of incubation. A single injection of 30 cc. of blood is recommended. Seventy-three per cent of the children receiving 6 cc. of serum from patients who had recently recovered were completely protected. Of sixteen children in whom the disease developed fourteen had it mildly. Whole blood or convalescent serum is of value in preventing and modifying both mumps and chickenpox. While whole blood does not prevent whooping cough, it modifies the disease and is of more value than whooping cough vaccine.

AIKMAN, Rochester, N. Y.

THE ACCESSORY NASAL SINUSES IN SCARLET FEVER. DONALD SMYTHE CHILDS, New York State J. Med. **33**:141 (Feb. 1) 1933.

It has not been generally taught that infection of the sinuses is a frequent accompaniment of scarlet fever, but in this study sinusitis was found in 91 per cent of 383 cases studied by roentgenograms. Seventy-nine per cent showed

hazing, and 12 per cent were opaque. The most frequent lesion was bilateral hazing of the maxillary and ethmoid sinuses, which occurred in 30 per cent of the cases; the next most frequent was bilateral hazing of the maxillary sinuses (27 per cent). Pansinusitis was present in 9 per cent. Exploration of the sinuses was made in but 1 case, and no pus was obtained. Ninety cases were restudied, and in only 12 per cent was there evidence of improvement; in 50 cases there was definite evidence of progression or extension of the roentgenographic evidence. Mastoiditis developed in 33 cases, and in each instance infection of the sinuses was shown on the same side.

AIKMAN, Rochester, N. Y.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES: JUNE 18 TO JULY 15, 1933. Pub. Health Rep. **48**:907 (Aug. 4) 1933.

During the four weeks previous to July 15 there was a total of 188 cases of poliomyelitis for the entire reporting area, as compared to 170 in 1932, 291 in 1931, 611 in 1930 and 133 in 1929, a normal year. The incidence of diphtheria and smallpox was the lowest recorded for this period in the five years for which data are available. Although the number of cases of scarlet fever was only half of that for the preceding four weeks and the incidence of typhoid fever was twice that of the preceding four weeks, both diseases were less prevalent than during the same period of last year.

The number of cases of epidemic meningitis was about the same as it was during the same month last year, except in Illinois for which 30 cases were reported. The incidence of measles and influenza dropped slightly more than the usual seasonal decline. The average death rate for all causes in large cities was 9.9 per thousand population, the lowest for this period in the eight years for which data are available.

LEMASTER, Evanston, Ill.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES: JULY 16 TO AUGUST 12, 1933. Pub. Health Rep. **48**:1069 (Sept. 1) 1933.

The number of cases of poliomyelitis increased from 188 for the four weeks ending on July 15 to 667 for the following four week period. Smallpox, diphtheria and meningococcic meningitis occurred at unusually low incidence. There was approximately the same number of cases of influenza, scarlet fever and measles as had been reported for the same period of recent years. The average mortality rate from all cases in large cities was 9.8 per thousand population.

LEMASTER, Evanston, Ill.

EXPERIMENTS ON THE PROTECTION OF MONKEYS WITH ANTIVACCINAL SERUM AGAINST THE VIRUSES OF VACCINIA AND VARIOLA. C. G. PANDIT, K. P. MENON, KHAN SAHIB and MOHAMAD OMAR SAHIB, Indian J. M. Research **19**:4 (April) 1932.

The serum used came from a buffalo employed to provide the lymph for inoculations. The animal was given three intravenous injections of the lymph, and seven days later the serum was obtained. This serum in the dilution of 1:40 completely inactivated an equal quantity of a 1:300 dilution of the vaccine lymph. Experiments in protection were carried out on monkeys. The same procedure was followed with the virus of variola and human convalescent serum. The antivaccinia serum from the buffalo protected the monkey if given before vaccination; administered with the vaccination it gave a variable degree of protection, and if given after the vaccination it afforded no protection. This serum, however, showed considerable protection when given four hours after the virus of variola, and a modified reaction if given twenty-four hours after the virus.

Serum from patients convalescent from smallpox gave a much higher degree of protection than immune serum from the buffalo.

SNELLING, Toronto.

CONVULSIONS IN WHOOPING COUGH. H. GRENET and E. MOURRUT, Arch. de méd. d. enf. **36**:585 (Oct.) 1933.

Convulsive seizures in the course of pertussis have been reported with increasing frequency since 1926. Grenet and Mourrut found, at the Bretonneau Hospital, during the year ending Oct. 1, 1932, 22 patients with convulsions in a series of 238, or nearly 10 per cent. Among etiologic factors, age was a preponderating element; all except 3 of the patients were under 2 years. In 9 cases the convulsions were initiated through the complication of pneumonia, usually of the bronchial type; in nearly half of the observations otitis media was the agent which precipitated the seizures and in 1 instance acute mastoiditis was found. Several cases were unquestionably encephalitic. The mortality among the 22 patients was 90 per cent. Autopsies on 15 of the children showed in several the typical findings of encephalitis, but most of them revealed simply congestion with edema. The theory that violent fits of coughing can mechanically produce cerebral hemorrhage is without basis, the writers assert.

AMESSE, Denver.

TETANUS OF UMBILICAL ORIGIN IN ALGERIA. GAUTIER, Bull. Soc. d'obst. et de gynéc. **22**:159 (Feb.) 1933.

Thirteen cases of tetanus were observed by the author during the winter of 1931-1932. All the cases occurred in natives during the rainy season. The occurrence among natives was probably due to the fact that the mothers are delivered in the squatting position, at times on the bare ground, and the cord is doubtless contaminated with infected soil. In order to reduce the incidence of the disease the author recommends education of the natives in regard to tetanus and European methods of delivery. Antitetanus serum might be injected as a prophylactic, or the mother might be immunized with tetanus antitoxin before delivery. Treatment of the disease with serum and the daily administration of chloroform is recommended. Two infants which were treated in this manner made a good recovery.

GLASER, Rochester, N. Y.

HYDROA VACCINIFORME. E. G. SCOLARI, Gior. ital. di dermat. e sif. **74**:241 (April) 1933.

Two cases of hydroa vacciniforme were studied in detail. In both cases coproporphyrin and uroporphyrin were found in the urine within normal limits. Likewise, the protoporphyrin content of the red blood cells was normal. The experimental production of lesions of hydroa in one of the patients by means of exposure to the sunlight and the internal administration of sulphonal was not followed by abnormal elimination of porphyrin. After exposure to the sun, the white blood cells suffered the same changes observed in normal persons under the same stimulus. The red cells showed a decrease when lesions of hydroa were produced by exposure to the sunlight, but when the experiment was unsuccessful the red cells increased, just as in normal persons. The blood sugar, blood nitrogen and bilirubin were also increased when the sunlight succeeded in causing the development of experimental lesions. Exposure of one of the patients to ultraviolet rays failed to produce lesions of hydroa, even after sensitization with acriflavine hydrochloride. Treatment with Finsen light under pressure was also unsuccessful. It is interesting to note that while the skin of the hands and face showed little reaction to the ultraviolet rays, the skin of the dorsum was quite sensitive to the same rays.

PARDO-CASTELLO, Havana, Cuba. [ARCH. DERMAT. & SYPH.]

SCARLET FEVER. KURT SCHIRLITZ, Dermat. Wchnschr. **96**:746 (June 3) 1933.

The author reviews the 106 cases of scarlet fever seen during the first nine months of 1932. The complications encountered were: disease of the kidneys,

53 per cent; disease of the ears, 22 per cent; rheumatism, 17 per cent; endomyopericarditis, 5 times, and thyroiditis, paratonsillar abscess and pulmonary abscess, each once.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

EPIDEMIOLOGIC, CLINICAL AND HISTOPATHOLOGIC EXPERIENCE DURING THE POLIOMYELITIS EPIDEMIC OF 1932 IN SILESIA. L. GUTTMAN, Med. Klin. **29**:939 (July 7) 1933.

In general, this article offers nothing new to any one who is familiar with the American literature on the subject. During 1932, poliomyelitis attacked 309 persons in Silesia. In accordance with the classic descriptions of such epidemics, the peak came in September, the disease was relatively more frequent in rural districts, and children between the ages of 2 and 5 years were conspicuously susceptible. Among the clinical signs, the author comments particularly on the retention of urine and feces and on the localized disturbances in sweating seen in certain cases. He describes one especially interesting case, that of a woman, 23 years old, who died of poliomyelitis on the sixth day of illness in the eighth month of pregnancy. Although the mother's spinal cord showed a severe specific inflammatory reaction, the baby's cord was normal.

DOOLEY, Kent, Conn.

TREATMENT OF ACUTE ARTICULAR RHEUMATISM AND OF SIMILAR INFECTIOUS DISEASES BY MEANS OF PAINTING WITH TANNIN SPIRITS AND INJECTION OF TURPENTINE OILS. A. STREUBEL, Med. Klin. **29**:1106 (Aug. 11) 1933.

This is a generalized and theoretical discussion of acute articular rheumatism. Streubel considers the disease to be due to streptococcic infection, the particular strain being as yet unidentified. He recommends painting the tonsils with alcohol or spirit of tannin in order to prevent further dissemination of bacteria or of bacterial toxins. This treatment is carried out three times a day, and is said to counteract fever and pains in the joints in those cases in which pains in the joints follow tonsillitis. Streubel has had good results with a nonspecific therapy which consists of intramuscular (gluteal) injections of a 10 per cent solution of turpentine in oleum arachidis (olobinthin) at intervals of two or three days: 1 cc. for adults, 0.5 cc. for children.

DOOLEY, Kent, Conn.

PLACENTAL EXTRACT AND SCARLET EXANTHEM. OTTO TEZNER and HELENE GOLDHAMER, Monatschr. f. Kinderh. **58**:388, 1933.

In a brief preliminary report of five cases, the writers confirm the work of Toomey and August that placental extract, when injected into the skin of a patient with scarlet fever, blanches the exanthem.

GERSTLEY, Chicago.

THE LATE EXANTHEM IN SCARLET FEVER. EBERHARD HUBENSACK, Monatschr. f. Kinderh. **59**:1, 1933.

In a review of his material of the last year Hubensack finds that late exanthems occurred in scarlet fever as actual recurrence of the disease and also as an erythema associated with the scaling.

Actual recurrence of the disease has occurred in only 5.9 per cent of his cases. Children under 6 years of age were predisposed. The recurrence appeared in the second or third week, was less severe than the original infection, had fewer complications and offered a good prognosis.

The typical postscarlatinal exanthem occurred associated with the scaling and unrelated to the intensity of the first infection. In frequency, it appeared in 56 per cent of the cases, and was observed chiefly during the second or third week. It involved points of the greatest mechanical liability, in various manifestations such as maculopapular, pityriasis-like, large papular, and so forth. It is independent of the severity of the disease and is treated by oiling the skin.

GERSTLEY, Chicago.

THE REACTION OF EOSINOPHILS TO INJECTION OF SCARLET FEVER ANTITOXIN. MAGDALENE HOLST, Monatschr. f. Kinderh. **59**:38, 1933.

After injection of scarlet fever antitoxin, it was found that the leukocyte count diminishes, that the eosinophils appear later and return to normal more speedily, and, further, that the increase in the number of eosinophils is not as great as in cases in which treatment is not given.

GERSTLEY, Chicago.

THE NORMAL AND THE ARTIFICIAL DIPHTHERITIC ANTITOXIN IN THE HORSE. B. FEIERABEND, Časop. lék. česk. **71**:195 (Feb. 12) 1932.

Most horses have native or normal diphtheritic antitoxin as a result of latent infection with diphtheria bacillus early in life. The titer of normal antitoxin is independent of the reactivity of the animal and the resistance to infection. In many cases, however, the normal antitoxin is proportional to the reactivity. The titer of the artificial antitoxin during the manufacture of antidiphtheritic serum is independent of the reactivity and in most instances is independent of the amount of normal antitoxin. The normal antitoxin increases with age, but the reactivity does not, so that older horses are not preferable. Arbitrarily, horses with less than 1/100 unit in 1 cc. of serum (40 per cent of horses) give 20 per cent usable serum, those with from 1/100 to 1/10 unit (40 per cent) give 60 per cent usable serum, and those with more than 1/10 unit (20 per cent) give 75 per cent usable serum. Selection of horses on the basis of normal serum (antitoxin) has some value, but direct titration of normal antitoxin is the best criterion.

STULIK, Chicago.

THE DURATION OF THE PERIOD OF INCUBATION OF HYDROPHOBIA AFTER THE HEALING OF THE ORIGINAL WOUND. CONSTANTINOV, Vrach. delo, 1933, no. 5, p. 239.

The author discusses the pathogenesis of hydrophobia with special reference to the period of incubation. He presents a case in which the period of incubation was six months. This was in a girl, 7 years old, with typical symptoms of hydrophobia and no injury other than a scar (3 cm. by 4 mm. in diameter) on the right leg, the result of a dog bite suffered six months previously, for which no antirabic treatment was given. There was some evidence of a recent inflammatory reaction in the region of the scar, namely, slight hyperemia and tenderness. The child died, and at autopsy typical Negri bodies were found in the brain.

Experiments proved the presence of virus in the old scar. A glycerin emulsion was prepared from a portion of the resected scar and injected subdurally into a rabbit with the result of typical symptoms of hydrophobia. An emulsion prepared from the normal skin of the dead child and injected similarly into rabbits did not produce the disease. An emulsion of the brain tissue of the same patient produced symptoms of hydrophobia in rabbits. Microscopic examination of the scar revealed the presence of Glugea lyssae or the microsporidian corpuscles which are so frequently found in nerve tissues of animals dying from hydrophobia. Constantinov believes these to be Negri bodies in earlier stages of development.

The conclusions are: 1. The virus of hydrophobia can remain at the original point of entry, i. e., in the scar tissue of an apparently healed wound, for as long as six months. 2. The virus is found there in the form of Glugea lyssae. 3. The virus, after remaining in a latent state for a variable length of time, can, in the presence of some unknown circumstance, spread and produce a generalized infection. 4. The sudden exacerbation of an inflammatory reaction in an apparently healed wound can thus be explained by the presence and activation of the virus locally.

BODER, Chicago.

Chronic Infections

THE ORIGIN OF THE EPITHELIOID CELL IN EXPERIMENTAL TUBERCULOSIS OF THE CORNEA. ESMOND R. LONG and SION W. HOLLEY, Am. J. Path. **9**:337 (May) 1933.

Infection of the center of the cornea of the rabbit with tubercle bacilli of the human type resulted in a lesion characterized almost solely by polymorphonuclear leukocytes until the appearance of new capillaries, when a rapid replacement of the polymorphonuclears by mononuclear phagocytic cells occurred. When two infecting doses were placed in the same cornea, one at the margin near the normal blood supply and one in the normally avascular center, the replacement of polymorphonuclears by large mononuclears occurred weeks earlier in the lesion close to the limbus.

The mononuclears which accounted for this replacement and functioning during the subsequent development of the lesion apparently arose from the primitive smaller mononuclear cells which were present in large numbers in and around the walls of the new capillaries. The source of these cells could not be determined with absolute certainty, but the following observations were evidence that most of them came from the blood stream: (*a*) Cells of similar character were present among the erythrocytes in the lumens of the blood vessels in great excess of the normal proportion; (*b*) migration figures of similar cells could be seen in the walls of the growing capillaries, and (*c*) mitotic figures were rare among them.

After accumulating in and around the capillary walls, the primitive cells underwent a progressive transformation by simultaneous increase in size and change into epithelioid cells, without mitosis.

AUTHORS' SUMMARY.

A COMPARISON OF THE CELLULAR REACTION IN EXPERIMENTAL TUBERCULOSIS OF THE CORNEA IN ANIMALS OF VARYING RESISTANCE. ESMOND R. LONG, SION W. HOLLEY and ARTHUR J. VORWALD, Am. J. Path. **9**:329 (May) 1933.

Injections of from 0.01 to 0.005 mg. of moderately virulent bacilli of the human type were made into the interlamellar spaces in the center of the cornea of normal and tuberculous guinea-pigs and of normal rabbits and cats, and the lesions were studied. The initial reaction was the outpouring of polymorphonuclear leukocytes, with a gradual replacement by large mononuclears after twenty-four hours. The reaction was most intense in tuberculous guinea-pigs; it was less in normal guinea-pigs, still less in rabbits and least intense in cats. This is in inverse relation to the general resistance of these animals to the strain of tubercle bacillus used.

MOORE, New York.

PURPURA HAEMORRHAGICA IN CONGENITAL SYPHILIS FOLLOWING ARSPHENAMINE. J. V. BICKFORD and R. C. TILGHMAN, J. A. M. A. **100**:1984 (June 24) 1933.

Two cases of purpura haemorrhagica in children with congenital syphilis followed the use of neoarsphenamine. The fact that these are the only instances of postarsphenamine dyscrasias of the blood among 1,825 children treated at the Harriet Lane Home for Invalid Children makes apparent the rarity of this sequela. The etiology is not clear.

BONAR, Salt Lake City.

TUBERCULOUS MENINGITIS. M. and MME. ANDRÈ JOUSSET, Bull. Soc. de pédiat. de Paris **30**:658 (Dec. 20) 1932.

Two hundred and twenty-five children between the ages of 1 and 5 years with tuberculous meningitis were treated by means of injections of a phosphatide extracted from tubercle bacilli. Fifteen of these, constituting 7 per cent, recovered. This phosphatide is extracted from a specially soluble type of tubercle bacilli. It

is a colloidal substance and thermolabile. It is toxic to a healthy animal. It is different from tuberculin. The dosage recommended is: 0.25 mg. for the first dose, followed in two days by 0.5 mg. and thereafter 0.5 mg. every four, five or six days. Improvement, when obtained, sets in soon after the first few injections —in fact, on the day following the first injection—in almost all the successful cases, so that one can usually foretell the fortunate result. The material is injected hypodermically, and this treatment is followed by lumbar puncture in a few hours to prevent increased intracranial pressure, which might ensue because of a possible increase in the secretion of cerebrospinal fluid.

All of the patients in the series reported on showed tubercle bacilli in the spinal fluid; a method for demonstrating them is given which consists of a double centrifugation of the fluid and staining of the sediment. The method is successful in nine of ten cases.

BENJAMIN, Montreal, Canada.

TUBERCULOUS CAVITY IN THE LUNG OF AN INFANT INVISIBLE ON ROENTGENOGRAPHIC EXAMINATION. LEON BERNARD, MAURICE LAMY and GAUTHIER VILLARS, Rev. de la tuberc. **13**:629 (June) 1932.

An infant, aged 12 months, showed a homogeneous diminution of transparency in the right supraclavicular and infraclavicular region. Autopsy revealed caseous degeneration of glands in the mediastinum and a large cavity at the apex of the lung. Thickening of the pleura and of its parenchyma prevented the detection of the cavity.

VINTON, Brooklyn.

IMMUNITY AGAINST TUBERCULOSIS AND THE TUBERCULIN REACTION. L. K. WOLFF, Nederl. tijdschr. v. geneesk. **77**:4084 (Sept. 9) 1933.

The first infection with a moderate quantity of tubercle bacilli gives rise in man to a tuberculous process that generally heals and yields a certain degree of immunity. This immunity can be interrupted under unfavorable circumstances, such as intercurrent diseases, insufficient nourishment or too strenous physical work. Then pulmonary phthisis may arise, either by activation of a slumbering process or by a new infection.

If the first infection occurs at an unfavorable time during the first year of life or in a person with decreased general resistance, or if the infection is too heavy, tuberculosis of the lungs may develop, which, however, is different, from a pathologic point of view, from pulmonary phthisis and has another course. To this category belong the tuberculosis of the youth in our country (the Netherlands), the tuberculosis of adults with a negative Pirquet reaction, who are running great risks of new infection, and the tuberculosis of the Javanese immigrants to Deli (the Dutch East Indies). Vaccination with Calmette's vaccine is as advisable for persons without immunity who come in contact with infection as for the infants of parents with open tuberculosis.

VAN CREVELD, Amsterdam, the Netherlands.

RESEARCH ON THE EXISTENCE OF VARIATIONS FROM THE NORMAL IN THE LUNGS OF APPARENTLY HEALTHY CHILDREN OF FROM SIX TO FOURTEEN YEARS OF AGE. M. H. TROMP and A. F. VAN WIERINGEN, Nederl. tijdschr. v. geneesk. **77**:4347 (Sept. 23) 1933.

The Pirquet test was performed on 1,000 healthy children from 6 to 14 years of age, belonging to all classes of the population of Utrecht. One hundred and forty-three children had positive reactions. Those of the first 500 children tested who gave positive reactions were extensively examined, and roentgenograms were made; those of the second 500 tested who gave positive reactions were examined by fluoroscopy, and if a variation from the normal was found, a roentgenogram was made. A control group with negative Pirquet reactions was examined in the same way as the second group. Of the 70 children in the first group who

had positive reactions, 21 required treatment, and of the 73 children of the second group, 10. The results are discussed in relation to the question whether the test is of value for the prognosis when some condition has been found that must be considered with regard to treatment and supervision. Furthermore, a system is proposed by which a greater prevention of tuberculosis can be obtained based on cooperation between medical inspectors in schools and the service for the prevention of this disease.

VAN CREVELD, Amsterdam, The Netherlands.

PROGNOSIS IN TUBERCULOSIS IN CHILDHOOD. J. LUNDQUIST, Svenska läk.-sällsk. handl. **59**:161, 1933.

In a reexamination of 926 children treated for tuberculosis from 1910 to 1920, Lundquist found that one fourth died from tuberculosis, three fourths of the deaths occurring during the first five years following the infection. The mortality curve showed two peaks, one for children infected in the first years of life and a lower peak for those infected at puberty. In cases involving the bronchial glands and in those showing massive parenchymal indurations the prognosis was favorable; it was less favorable in cases showing roentgenologically demonstrable disseminated parenchymal indurations. Of children with a positive reaction to tuberculin who did not have certain clinical or roentgenologic changes, 16.4 per cent died from tuberculosis. In open tuberculosis the prognosis was grave, with a mortality of 86.9 per cent, 60 per cent of the children dying within the first year and 86.3 per cent within the first three years after demonstration of tubercle bacilli in the sputum; 84.5 per cent of these patients were approaching or at the age of puberty, and there were twice as many girls as boys. Whooping cough and scarlet fever had no noticeable effect on the tuberculous process, whereas measles usually caused a transient aggravation.

ELGHAMMER, Chicago.

RATE OF RED CELL SEDIMENTATION IN CASES OF TUBERCULOSIS IN CHILDREN. A. FRIEDLAENDER, Ugesk. f. læger **95**:896 (Aug. 24) 1933.

Repeated determinations of the rate of red cell sedimentation according to Langer and Schmidt's micromethod were made by Friedländer for 100 children with a positive reaction to tuberculin. He concludes that a constant increase in the rate indicates an active process and an unfavorable outcome. Normal sedimentation in the case of a child with a positive Pirquet reaction, unless the clinical examination otherwise discloses signs of an active process, indicates a dormant process.

ELGHAMMER, Chicago.

LOW RED CELL SEDIMENTATION IN CASES OF PULMONARY TUBERCULOSIS. A. FREUDENTHAL, Ugesk. f. læger **95**:957 (Sept. 7) 1933.

Freudenthal emphasizes that, while determination of the rate of red cell sedimentation is an excellent supplementary procedure among the general methods of examination, normal sedimentation is not a certain indication of inactivity and cannot be recommended as decisive in doubtful cases.

ELGHAMMER, Chicago.

Internal Diseases

HEART DISEASE IN GENERAL PRACTICE. J. V. DEPORTE, Am. Heart J. **8**: 476 (April) 1933.

This article is a statistical study dealing in the main with adult conditions. A few interesting facts, however, are stated about children. In 1928, heart disease was ninth in importance among the causes of death of children between 1 and 10 years of age; in those between 10 and 15 years, it was second in importance. The leading etiologic factors in deaths of children under 20 years of age were rheumatic

infection, other acute infections and congenital infections in the order named. Under 10 years, the etiologic factors were rheumatic disease, 70 per cent; congenital disease, 20 per cent, and miscellaneous infections, 10 per cent.

BACHMANN, Chicago.

SO-CALLED ALLERGIC MANIFESTATIONS AND THE INCIDENCE OF RESPIRATORY INFECTIONS IN RHEUMATIC AND IN NON-RHEUMATIC CHILDREN. C. C. MCLEAN, Arch. Pediat. **50**:123 (Feb.) 1933.

With the idea of proving or disproving the conception that rheumatic fever is probably an allergic response in the body to an active focus of infection, McLean reports the incidence of so-called allergic manifestations in seventy-two children. He divides them into two groups: thirty-six rheumatic and thirty-six nonrheumatic subjects. All allergic manifestations and respiratory infections observed in each rheumatic child from the age when first seen by the physician to the age of the first known manifestation of the rheumatic infection are tabulated and compared with those of a nonrheumatic child born in the same month and year, who has been observed for an equal period of time. Eczema, urticaria, spasmodic croup and asthmatic bronchitis were considered as allergic manifestations. It appeared that so-called allergic manifestations were no more prevalent in the rheumatic than in the nonrheumatic children, with the possible exception of gastrointestinal symptoms complicating respiratory infections, if such symptoms can be considered as an allergic manifestation. The incidence and severity of respiratory infections differed little in the rheumatic and the nonrheumatic children.

WADDELL JR., University, Va.

CRYSTALLINE INSULIN IN THE TREATMENT OF DIABETES MELLITUS. JOHN EAGER HOWARD and AGNES DELAWDER, Bull. Johns Hopkins Hosp. **52**:173 (March) 1933.

A series of four diabetic patients were regulated on diets and commercial insulin under most careful supervision. Crystalline insulin was then substituted for commercial insulin in equivalent doses.

Apart from slight increases in the tolerance for carbohydrates, which might be expected in diabetic patients under treatment, no appreciable difference could be detected clinically between the periods during which commercial insulin was injected and those during which crystalline insulin was injected.

When injected in equivalent doses into human subjects suffering from diabetes mellitus, crystalline insulin gives the same therapeutic effects as commercial preparations of insulin.

AUTHORS' SUMMARY.

SOME OBSERVATIONS ON THE VALUE OF INTRATRACHEAL INJECTIONS OF IODIZED OIL FOR BRONCHIAL ASTHMA. WILLIAM ANDERSON, J. Allergy **4**:44 (Nov.) 1932.

This article presents a preliminary report of observations on sixty cases of bronchial asthma. The patients were all over 12 years of age, and the attacks, except in one instance, had existed for from four to forty-eight years. Sensitiveness to foreign proteins was present in about one half of the cases. In the others, the attacks were due to peripheral or psychic causes or to infection of the respiratory system.

The amount of oil, the frequency of the injections and the area of the lungs into which the injections were made varied with each patient. Twenty-four of the sixty patients have been relieved for from one to five and one-half years. The other thirty-six have all been relieved, having been under treatment for from three to twelve months. There was a rapid decrease, owing to clinical hypersensitiveness to foreign proteins. Infections of the respiratory tract responded less rapidly.

The obstructions in the lumen of the bronchial tubes caused by coagulated mucus disappeared after sufficient contact with the iodized oil; the improvement of the patient depended on the disappearance of the plugs of mucus.

The work is being continued, and other matters of interest such as the freedom of symptoms and their relation to cutaneous sensitivity to various specific asthmatic excitants are being studied.

HOYER, Cincinnati.

OBSERVATIONS ON THE FORMATION OF WHEALS: VI. RESPONSE OF NORMAL AND ALLERGIC INDIVIDUALS. F. S. MCCONNELL, J. Allergy **4**:177 (March) 1933.

The experiments conducted showed a great variation in the size of the histamine wheals caused by injections into the upper outer part of the arm of normal persons at different intervals. The histamine wheals of patients having bronchial asthma, vasomotor rhinitis, urticaria, angioneurotic edema or headache were distinctly larger during an attack than they were between attacks. The wheals in the sensitive normal persons showed no appreciable difference during and between attacks.

HOYER, Cincinnati.

THE USE OF SUPRARENAL CORTEX EXTRACT IN BRONCHIAL ASTHMA. A. H. FINEMAN, J. Allergy **4**:182 (March) 1933.

Four patients having bronchial asthma for a period ranging from six months to eighteen years were given injections of suprarenal cortex subcutaneously and intramuscularly for periods ranging from six weeks to four months. One patient showed marked improvement, one moderate, one slight, and one no improvement. There were a decided increase in the strength and the appetite of three of the four patients and an average gain in weight of 4½ pounds (2 Kg.). There was no appreciable change in the blood pressure, and there was no influence on the pulse rate during, or at the end of, the course of treatment.

HOYER, Cincinnati.

BLOOD CULTURES IN CHRONIC ARTHRITIS. E. F. TRAUT, J. Infect. Dis. **52**:230 (March-April) 1933.

The blood cultures of 71 per cent of thirty-eight patients with chronic arthritis were positive for enterococci, which in the early stage of isolation resembled the G colonies of Hadley.

TOOMEY, Cleveland.

BACTERIOLOGIC INVESTIGATION OF THE BLOOD IN RHEUMATIC FEVER: PRESENTING EVIDENCE OF DISSOCIATION OF MICRO-ORGANISMS RECOVERED FROM BLOOD CULTURES. BESSIE R. CALLOW, J. Infect. Dis. **52**:279 (May-June) 1933.

Callow reviews her work on blood cultures in rheumatic fever and concludes that diplostreptococci of the alpha type and pleomorphic bacilli may be found not only in rheumatism, but in certain diseases of the upper respiratory tract. She decides that these bacteria represent different life stages of the same organism. She questions the relationship between these organisms and rheumatism. This article is a compendium of the knowledge on the subject. There is also included a complete plan of attack, together with a close description of methods. It is a convincing report.

TOOMEY, Cleveland.

VEGETAL (PEANUT) BRONCHITIS. RICHARD L. BOWER, J. Missouri M. A. **30**:7 (July) 1933.

Vegetal bronchitis is caused by the inspiration into the lower air passages of various substances of vegetal origin, such as peanut kernels, other nut kernels,

beans, watermelon seeds, corn and fruit seeds. The results are worse in very young children.

The initial symptoms are choking, gagging, coughing and wheezing. There is then usually a quiescent period free from symptoms, owing to the fixation in the air passages of an unobstructive foreign body. Bodies freely movable in the bronchi cause more irritation, edema and symptoms and are most dangerous.

Later symptoms depend on whether there is complete obstruction or inspiratory or expiratory obstruction. With a movable body the three cardinal signs of Jackson appear, namely, an "audible slap," a "palpatory thud" and an "asthmatoid wheeze." If the obstruction is expiratory only, an emphysema distal to the obstruction appears. If the obstruction is complete, atelectasis is present beyond the obstruction.

Displacement of the heart and mediastinum and the position of the diaphragm as shown by roentgen examination are important diagnostic aids.

The treatment is bronchoscopic removal of the foreign body without anesthesia (except for swabbing with 10 per cent cocaine and epinephrine). Tracheotomy is recommended after bronchoscopy in order to permit better removal of the thick, tenacious mucus which the child cannot cough up. This is particularly true when the foreign body is a peanut kernel and if possibly a small portion remains in the bronchus. The peanut is by far the most dangerous substance because of an acid present in both the oleic and the linolic fractions of the fatty acid of the nut.

Several good roentgenograms accompany the article.

BERGER, Kansas City, Mo.

THE LIPOID DEGENERATIVE DISEASES. CARROLL M. POUNDERS, J. Pediat. **2**:216 (Feb.) 1933.

A discussion of the etiology, pathology and clinical course of infantile amaurotic family idiocy (Tay-Sachs' disease) and essential histiocytosis (Niemann-Pick's disease) is presented. A typical case of each condition in non-Jewish families is reported.

LEMASTER, Evanston, Ill.

OSTEOMALACIA. GERARD N. KROST, J. Pediat. **2**:553 (May) 1933.

In the case of a boy, aged 10 years, with severe skeletal deformities and marked rarefaction of the bones the diagnosis was osteomalacia or late rickets. At 2 years of age there had been abdominal enlargement and diarrhea which lasted for one year. From the time of weaning practically no milk and very few vegetables were taken. Ultraviolet irradiation and large doses of viosterol failed to produce improvement. Death was due to nephrosis.

LEMASTER, Evanston, Ill.

SINO-AURICULAR HEART-BLOCK IN CHILDHOOD. GUSTAVE F. WEINFELD, J. Pediat. **2**:559 (May) 1933.

A case of sino-auricular heart block in a 6 year old child is reported, with a review of the literature on this condition. The disappearance of the block after large doses of atropine, the associated sinus arrhythmia of marked degree and the absence of other etiologic factors indicated that an abnormal exaggeration of the physiologic activity of the vagus was the cause of the irregularity. In this patient there were no symptoms from the sino-auricular block. After thirty months of observation the condition persisted without change.

LEMASTER, Evanston, Ill.

CHRONIC SIALODOCHOPAROTITIS WITH RECURRENT SUBACUTE EXACERBATIONS. SOL LONDE and MORT D. PELZ, J. Pediat. **2**:594 (May) 1933.

A case of chronic sialodochoparotitis in a boy, aged 10 years, is reported, with a complete review of the literature on this condition. For two and one-half years

the patient had periodic painful swelling of the left parotid gland every three or four months. The roentgenogram taken after the injection of iodized poppy seed oil 40 per cent into Stenson's duct showed dilatation of the smallest secretory ducts throughout the gland. Improvement during one attack followed intramuscular injections of milk.

LeMaster, Evanston, Ill.

Ileocecal (Enterogenous) Cyst. C. E. Bradley and C. C. Hoke, J. Pediat. **2**:614 (May) 1933.

The authors add one more case of enterogenous cyst to the twenty-eight cases already reported in the literature. The patient was a boy, aged 6 months, who showed signs of partial obstruction of the bowels and a palpable mass in the right lower quadrant of the abdomen. At operation a thick-walled cyst, 5 cm. in diameter, filled with clear mucoid fluid, was found in the wall of the terminal ileum, immediately external to the mucous membrane. The entire cyst was not removed because of the danger of weakening the wall of the bowels. Eighteen days after leaving the hospital the same symptoms returned. At this time a radical resection of the terminal ileum and cecum was performed, followed by complete recovery.

LeMaster, Evanston, Ill.

Peptic Ulcer in Children. Roger L. J. Kennedy, J. Pediat. **2**:641 (June) 1933.

Six cases of peptic ulcer in childhood are reported. The youngest children in the series were 4 and 6 years of age. The authors state that, regardless of the age of the child, a complaint of epigastric pain which occurs sometime after meals, particularly at night, and which is relieved by the ingestion of milk or by emesis and is accompanied by tenderness in the right upper part of the abdomen should lead to a strong suggestion of peptic ulcer and should be an indication for roentgenologic examination of the stomach and duodenum. Ulcers in infants up to 1 year of age are usually acute and are most commonly suspected because of melena. Indications for medical and surgical treatment of ulcer and its complications are essentially the same in children as in adults.

LeMaster, Evanston, Ill.

Management of Pyloric Obstruction in Infancy. Harry Lowenburg, Pennsylvania M. J. **34**:494 (April) 1931.

After a clinical experience extending over twenty years and the study of one hundred cases of pyloric obstruction in infants, the writer believes that spasm plays the greater rôle, is always present and precedes the hypertrophy; he suggests that the designations "congenital" and "hypertrophic" be discarded and replaced with the term "pyloric obstruction incomplete," "pyloric obstruction surgical," or "pyloric obstruction nonsurgical." On the basis of this conception, he has worked out a method of nonsurgical treatment and management of pyloric obstruction in which Sauer's thick cereal mixture is employed, not as an inflexible formula but adaptable to variation to meet the indications in individual cases. The observation that the incidence of pyloric obstruction is seasonal, occurring in the spring and fall, and is frequently associated with hypertonia, especially in males, led to the employment of magnesium hydroxide in ascending doses, subcutaneous injections of 1 cc. (20 units) of parathormone on alternate days and, as further possibly useful therapeutic measures, the administration of viosterol and exposure to ultraviolet radiation with the mercury vapor arc in quartz. He no longer administers atropine to these patients.

Hall, Uniontown, Pa.

ANALYSIS OF THE SYNDROME OF PRECOCIOUS MENSTRUATION. THEODORE O. ELTERICH, Pennsylvania M. J. **34**:629 (June) 1931.

The author reports the case of a 4 year old child showing precocious menstruation, early puberty and premature skeletal ripening. The physical attributes were strikingly feminine in type. Mental tests computed on the Merrill-Palmer scale placed the mental age at 27 months. Gynecological examination revealed that the uterus was considerably more than one-third the size of that of an adult; the right ovary was 3 cm. in diameter, and the left ovary was not palpable; there were enlarged, rounded breasts, pelvic widening of the hips and enlarged genitalia with pubic hair. All laboratory findings were negative. Menstruation began at the age of 18 months and recurred at monthly intervals. A review of the literature is followed by a discussion of what constitutes precocious menstruation, the etiology and differential diagnosis of the condition, osseous development in precocious puberty, precocious pubescence and mental growth, early pregnancy and the treatment of precocious menstruation. The author concludes with a tabulation of twenty-five cases from the literature that came to operation or necropsy, recorded with reference to the author reporting each case, the age of the patient, the physical manifestations, the gross and microscopic pathologic changes and the outcome.

HALL, Uniontown, Pa.

PYLOROSPASM DUE TO ALLERGY, SIMULATING INFANTILE PYLORIC STENOSIS. R. M. BALYEAT and C. M. POUNDERS, South. M. J. **26**:436 (May) 1933.

The foods to which a child is specifically sensitive may appear in the mother's milk in sufficient quantity to cause violent abdominal symptoms. A child may clinically be extremely sensitive to two or more foods, acquiring a complete or practical tolerance to one and retaining a marked sensitization to others. A patient may be skin-sensitive to many foods, but clinically sensitive to only one. A diagnosis of hypertrophic pyloric stenosis is not justified in a child in whose family allergy occurs or who suffers from some allergic manifestation, until allergy has been ruled out as a possible cause of the stenotic symptoms. The pediatrician and surgeon should not forget that sensitization to foods is a cause of pylorospasm which may simulate closely infantile pyloric stenosis.

SCHLUTZ, Chicago.

THE HEART IN INFANCY AND CHILDHOOD. RAYMOND M. SLOAN, West Virginia M. J. **29**:226 (May) 1933.

Heart disease is discussed from the standpoint of public health and of prevention. It continues to be the leading cause of death in the United States, standing fourth as a cause of death among school children. Within fifty years deaths from tuberculosis have declined over 40 per cent, while those from heart disease have increased over 40 per cent. It is estimated that fifteen of every 1,000 children have heart disease. It is more common in urban districts than in rural districts and more common in the North than in the South.

Cardiac lesions are preventable but are not curable. They may be divided into three groups according to their cause: rheumatic, syphilitic and degenerative and senescent. Practically every death due to cardiac disease in persons under 40 years of age (which group comprises 25 per cent of all the deaths due to this cause) is directly traceable to rheumatic fever in childhood. Rheumatic fever involves practically every tissue of the body. Early clinical manifestations are often lacking, and watchfulness is essential. Foci of infection should be eradicated. Congenital lesions of the heart should be carefully studied. Their incidence may be reduced by prenatal care. Sloan believes that there should be more careful supervision of the pupils in high schools and in junior high schools to prevent injury to the heart in physical activities and in competitive sports.

SHAWKEY, Charleston, W. Va.

OTITIS MEDIA AS AN AETIOLOGICAL FACTOR IN GASTRO-ENTERITIS. LEONARD FINDLAY, Arch. Dis. Childhood **7**:307 (Dec.) 1932.

Otitis media has been stressed as a factor in the etiology of gastro-enteritis. The author feels that otitis is not the important factor, but it may develop during the course of gastro-enteritis and increase the gravity of the case. Broncho-pneumonia or pyelonephritis also may develop during the course of nutritional diseases, but gastro-enteritis is the major problem and demands first consideration.

KELLY, Milwaukee.

CRANIO-HYPOPHYSEAL XANTHOMATOSIS. JOHN FRASER, Tr. Med.-Chir. Soc. Edinburgh, 1933, p. 25, in Edinburgh M. J., Feb. 1933.

Professor Fraser reports a case of Christian-Schüller's disease in a boy aged 3 years. The first evidence of disturbance was at the time of dental eruption, when the teeth crumbled and became infected as soon as they appeared above the gums. At 1 year of age, underdevelopment was manifest. During the second year the child was sick and irritable, and during the succeeding months he frequently held his left ear as if in pain. A fluctuating tumor then appeared above the ear; the swelling on aspiration showed bloody fluid. At 3 years the head was larger than normal, and the eyes were prominent. A roentgenogram of the skull showed an absence of bone on the left side, involving the region of the greater wing of the sphenoid, the temporal bone and the left half of the occipital bone. This corresponded to the area of soft and semifluctuant tissue, which proved to be pulsating brain tissue. Independent circular points where the bone was absorbed were found at a higher level.

The condition partakes of the nature of tumor formation affecting the reticulo-endothelial tissues, which goes on to further absorption of the skull. The entire skull may become gelatinous. The tuber cinereum and pituitary glands may be infiltrated, resulting in diabetes insipidus and dwarfism. Invasion of the optic tract causes exophthalmos. Other bones of the body may be involved. In the acute cases the prognosis is unfavorable. Roentgen therapy seems to be of benefit. The appearance of the tumor is that of xanthomatosis.

NEFF, Kansas City, Mo.

A CASE OF HAEMANGIO-LYMPHANGIOMA OF THE NECK OF THE CHILD CAUSING DELAY IN LABOR. R. W. JOHNSTONE, Tr. Obst. Soc. Edinburgh, 1933, p. 44, in Edinburgh M. J., April 1933.

Tumors of the neck are not commonly recognized at birth. Goiter sometimes exists at birth. Any tumor of the neck causing delay in labor is rare. The writer reports the case of an infant born after twenty-four hours of labor in whom a semicystic tumor was present which varied in appearance from crimson to pallor, owing to the fact that it was a hemangio-lymphangioma. Since birth the tumor has grown larger, and infiltrates the floor of the mouth, pushing up the tongue. Nursing is interfered with so that spoon feeding is necessary. An operation is contemplated at any early opportunity.

NEFF, Kansas City, Mo.

STUDIES IN URINARY INFECTION, THERAPEUTIC AND BACTERIOLOGICAL. D. MELVILLE DUNLOP and I. LAWSON DICK, Tr. Med.-Chir. Soc. Edinburgh, 1933, pp. 74 and 83, in Edinburgh M. J., May 1933.

These experimenters show that ketonuria has a bacteriostatic effect not explained on the basis of an increase in urinary acidity. A certain degree of acidity is not as yet proved as essential. The active substance is not known.

NEFF, Kansas City, Mo.

PATHOGENESIS OF RENAL DWARFISM. M. SENDRAIL and P. BEZY, Arch. de méd. d. enf. **36**:407 (July) 1933.

It is generally admitted that a chronic lesion of the kidney may retard development and provoke a condition of generalized dystrophy. Until recently this syndrome was not recognized by many French clinicians, although isolated cases were reported by Hutinel and others. Alpert has also described four of these rare cases within four years.

In adding two further observations the authors discuss at length the various theories concerning the pathogenesis of this strange disorder. They attempt to refute the hypothesis of Mitchell and others of the American school who advance the opinion that the etiology of renal rickets is concerned primarily with the excretion of endogenous phosphates by the intestinal mucosa, where the absorption of calcium is prevented through the formation of insoluble calcium phosphates, resulting in a true calcium starvation of the skeleton. The theory of pluriglandular disturbances in the origin of this specific type of nanism is also scouted.

As this specific dystrophy is concerned entirely with the osteogenic functions and as renal dwarfism is essentially osseous dwarfism, the authors suggest that the present designation be changed to "the osteorenal syndrome" to avoid any implication of hormonic disequilibrium.

In the endeavor to determine what factor, humoral or toxic, might be incriminated in the physiopathologic mechanism of this syndrome, it is recalled that rachitic disturbances of early infancy are accompanied by an intense acidosis, which, according to Blum, Delaville and van Canlaert, is entirely responsible for the phenomenon of decalcification. Certain continental writers have declared for a similar etiology in various osteopathies of the young, as well as in osteomalacia, osteospongiosis, localized dystrophy of the osseous capsule of the labyrinth, etc. It would appear, therefore, that in the majority of cases imperfections of osseous development are due to disturbances of the acid-base equilibrium.

It is admitted that the disorder studied may be due to a functional derangement affecting the kidney alone; innumerable investigations have proved the existence of acidotic nephritis (Rathery, Jeanbran and Cristol, Roque and Delore, Cordier and others).

In the evolution of the syndrome of nitrogen retention particularly, the progressive decline in the alkaline reserve has frequently been noted and has been interpreted by some, especially certain American observers, as due to a renal impermeability for phosphates. While this theory has manifestly much to commend it, the majority of clinicians believe that the attack on the ammonium-producing function plays the essential rôle. The authors interpret this variety of dwarfism as an osteodystrophy from renal acidosis.

AMESSE, Denver.

ORTHOSTATIC ALBUMINURIA. P. NOBECOURT, Progres méd., April 22, 1933, p. 726.

Orthostatic albuminuria is seen in thin children who have lordosis and who are between the ages of 6 and 10 years. It is caused by passive congestion of the kidneys. There are no symptoms except albuminuria. The albumin disappears if the child is put at rest. The condition never predisposes to a pathologic condition of the kidneys, and recovery is spontaneous.

SANFORD, Chicago.

CLINICAL SIGNIFICANCE OF ALTERATION OF MUSCLE TONE IN CHILDREN. SIEYRO, Galicia clin. **5**:129 (April 15) 1933.

Hypotonia occurs in all pathologic conditions when there is interruption of the sensory paths by which muscular tone is maintained, and especially when the interruption involves the anterior horns of the medulla as well as the peripheral nerves. It is seldom found in the juvenile tabes of infancy and in adolescence. In hypotonia it is known that the lesions are caused by atrophy of the posterior roots and sclerosis of the posterior fibers. In tabes the hypotonia is pronounced. The muscles become pale and flaccid and offer little resistance to forces exerted on

the limbs, allowing the limbs to be distorted into shapes impossible for normal persons to assume.

Another disease in which hypotonia is seen is hereditary ataxia, or Friedreich's disease, characterized by weakness of the limbs and incoordination, the ataxia affecting successively the lower limbs, the trunk, the upper limbs, the functional muscles and the eyeballs. The sensory nerves and the sphincters are free from involvement. In Friedreich's disease hypotonia is a constant symptom and is slowly progressive. The lesions are located chiefly in the posterior fibers, the column of Goll being changed more than that of Burdach. Frequently the posterior spinal roots are affected, the anterior roots remaining normal.

Sometimes hypotonia appears when the anterior rootlets of the medulla are affected, as in poliomyelitis in which the anatomic lesion consists of myelomalacia of the anterior horns caused by endarteritis. This is the primary lesion; those of the nerves, muscles and bones are secondary. Hypotonia is much accentuated in infantile paralysis, and this, together with relaxation of the articular ligaments, causes the well known puppet dance in the limbs.

In polyneuritis, too, diminution of muscle tone occurs for the same reason. Hypotonia of sensory origin is accompanied by altered sensation and ataxia, and that of motor origin by paralysis and atrophy. Besides the numerous congenital forms of amyotonia, Oppenheim described in 1900 a disease characterized by extreme flaccidity of the muscles without atrophy, which is most marked at birth and diminishes slowly and progressively from then on. It is now believed that Oppenheim's amyotonia is due to prenatal poliomyelitis.

VINTON, Brooklyn.

LIPOID GRANULOMATOSIS (HAND-SCHÜLLER-CHRISTIAN'S DISEASE). VON W. C. CEELEN, Deutsche med. Wchnschr. **59**:680 (May 5) 1933.

The author describes the case of a child, aged 2 years, who acquired a peculiar rash; within three months he lost the ability to walk, complained of pain in the joints and lost some of his teeth. Multiple defects in ossification developed on the skull, the clavicles and some of the ribs, and the child died. Autopsy showed multiple sulphur-red, slightly hemorrhagic foci of destruction in the skull, scapula, ribs and clavicles and many of the long bones. Similar yellow lesions were found on the pleurae, lungs, fat tissue, liver, spleen, suprarenal glands and lymph glands. The histology showed destruction of the bone with the formation of granulation tissue. In the granulation tissue the lipoid cells (xanthoma cells) dominated. Fat staining showed the presence of lipoids, neutral fats and fats in crystal form.

Ceelen thinks that the disease described belongs to the group of diseases due to disturbance in the lipoid metabolism. The outstanding feature is granulation lipoidosis. The pathogenesis of the disease consists in destructive granulation with a secondary accumulation of lipoid. The author quotes L. Pick, who claims that four diseases belong to the group of primary disturbance of the lipoid metabolism. They are: (1) Gaucher's disease, (2) Niemann-Pick's disease (3) Hand-Schüller-Christian's disease and (4) xanthomatosis.

KERESZTURI, New York.

SCHÜLLER-CHRISTIAN'S SYNDROME: REPORT OF A CASE. W. HERZAU and H. PINKUS, Klin. Monatsbl. f. Augenh. **89**:721 (Dec.) 1932.

Schüller, in 1915, and Christian independently, in 1919, described a disease which was characterized by defects of the cranium, exophthalmos and diabetes insipidus. Rowland, in 1928, discovered disturbance of the lipoid metabolism as the etiology of this syndrome, which he therefore classed as disseminated xanthoma, and which Chester classed as lipoidogranulomatosis. Other terms are Hand's disease, Gaucher's disease and Niemann-Pick's disease. Folke Hensen compiled fifty-four cases, including three of his own observation; he termed the syndrome a special form of general xanthomatosis.

Herzau and Pinkus report the case of a boy, aged 6, who showed symptoms of polydipsia and polyuria, together with mental changes from the third year of life

on. Later, enormous enlargement of the penis, adiposity and enlargement of the liver occurred. The ocular symptoms were an ulcer and an osseous fistula at the temporal canthus of the left eye, and exophthalmos, which increased from 2 to 7 mm. within two years' observation. A defect of the skull was felt in the median line above the lambdoid suture. Several smaller defects were discovered in the roentgenogram. No defect involved the internal table; the typical "map-shaped" appearance of the skull was absent, but the rarefaction progressed. The Wassermann and tuberculin reactions were negative, and hypercholesteremia was absent.

Histologic examination revealed a xanthoma, with foam cells, giant cells and lipoid macrophages. The elephantiasis of the penis, observed in this syndrome for the first time, was probably caused by xanthomatous processes which caused stasis of the lymph.

STOLL, Cincinnati. [ARCH. OPHTH.]

UNDULANT FEVER IN CHILDREN WITH LYMPHOGRANULOMA. M. MEYER, Ztschr. f. Kinderh. **54**:631, 1933.

The author gives the report of a case of an undulant type of fever in a child, aged 9 years. The symptoms were first noted at 4 years, but they were vague and characterized only by temporary glandular enlargement. The peculiar fever occurred later. After serologic tests proved to be negative for malaria, Bang's disease, typhus and similar infections, biopsy was performed and lymphogranuloma was considered to be the most likely diagnosis. Other cases are collected from the literature.

SHELLING, Baltimore.

AN INSTANCE OF OSTEOGENESIS IMPERFECTA CONGENITA. Y. KATSU, Jap. J. Obst. & Gynec. **16**:171 (April) 1933.

The author mentions two types of congenital abnormality of the fetal skeleton: osteogenesis imperfecta congenita and chondrodystrophia fetalis. Osteogenesis imperfecta is characterized by impaired ossification arising from periosteal developmental disturbances and immature osteoblasts; the bones are slender and are subject to fracture; the epiphysis is normal, and therefore the length of the bones is normal. In chondrodystrophia fetalis an inhibition of cartilaginous development and a disturbance of intracartilaginous ossification are the characteristic signs; the development of the ends of the long bones is greatly disturbed, but periosteal ossification is normal, the bones becoming short and thick.

Clinically, the most characteritsic sign of osteogenesis imperfecta is the presence of a remarkably soft cranium; the possible causes of this disease are hereditary abnormalities of the endocrine system and nutritional disturbances.

A case of osteogenesis imperfecta is reported in a 23 year old primigravida; the fetus weighed 2,850 Gm., and the aforementioned signs were clearly demonstrated; efforts at resuscitation were fruitless.

ARNOLD, Chicago.

COLDS AND THE TEMPERATURE OF THE AIR. J. J. VAN LOGHEM, Nederl. tijdschr. v. geneesk. **77**:289 (Jan. 21) 1933.

The author draws attention to a report by Frost and Glover, published by the American Public Health Service. This report deals with the synchronism of epidemic fluctuations of colds as recorded in different cities in various parts of North America (Boston, Chicago, Columbia, Washington, San Francisco and New Orleans). Frost and Glover give no explanation for this synchronism. They point out that the climatic conditions in the places concerned in the inquiry differ so widely that the temperature of the air deserves no consideration as a causal factor. Van Loghem does not subscribe to this view. He believes that in America as well as in Holland (*J. Hyg.* **28**:33, 1928) local fluctuations in the temperature of the air are related to epidemics of colds. The results of an inquiry made by the author in Holland are in contradiction to those of the American investigation.

VAN CREVELD, Amsterdam, The Netherlands.

Nervous Diseases

TUBERCULOMA OF THE BRAIN, WITH A REPORT OF FOUR CASES. ERNEST SCOTT and GRANT O. GRAVES, Am. Rev. Tuberc. **27**:171 (Feb.) 1933.

The cases reported are those of cerebellar tuberculoma in a man, aged 37; left cerebellar tuberculoma, with spinal meningitis, in a boy aged 3½ years; pontile tuberculosis in a man, aged 20, and right cerebellar tuberculoma in a woman, aged 25. In this article the literature is reviewed and the reported cases are brought up to date.

Infectious material is carried to the brain from some focus by the blood stream. The areas which receive a majority of the infected blood at first hand and those which are supplied predominantly by the vertebral arteries are the ones most frequently attacked, viz., the cerebellum and the pons; the frontal, central, paracentral and occipital areas, and the corpus striatum. Tuberculomas comprise about 2.5 per cent of all tumors of the brain and occur twice as frequently in males as in females. They are found in 49.5 per cent of the cases of tumor of the brain occurring before the age of 10 years and in 9 per cent of the cases occurring in the next three decades. The solitary type is twice as common as the multiple. Tuberculomas occur with almost equal frequency in the cerebrum and the cerebellum, but localization in the cerebellum is four times as frequent as in any division of the cerebrum.

EUGENE SMITH, Ogden, Utah.

RELATIONSHIP BETWEEN TRAUMA SUSTAINED AT BIRTH AND ENCEPHALITIS IN CHILDREN. SOL ROY ROSENTHAL, Arch. Path. **16**:33 (July) 1933.

The clinical course and the pathologic findings of encephalitis occurring in three children of one family are discussed. The primary condition was thought to be due to trauma at birth, while the recent changes were infectious or toxic. It is suggested that many of the idiopathic and atypical forms of encephalitis in children are due to the superimposition of mild infection or intoxication in a brain in which the resistance has been lowered by trauma at birth.

LEMASTER, Evanston, Ill.

FACIAL REFLEXES. SAMUEL M. WEINGROW, Arch. Pediat. **50**:234 (April) 1933.

Several new facial tendon or myotatic reflexes are described. These reflexes were found in normal persons and have been noted in children of all ages. In tetany they are markedly exaggerated in the form of Chvostek's sign. In addition to the usual facial reflexes, a winking reaction having a number of afferent connections is described. This is shown to be definitely affected in conjunction with other facial reflexes in Bell's palsy and in encephalitis lethargica. Cases of cerebral palsy, meningo-encephalitis and traumatic or infectious involvement of one or both facial nerves in which the facial reflexes are markedly affected are also described. In diseases of the brain and of the cranial nerves these reflexes show variations from the normal and thus serve to support the diagnosis of these diseases.

WADDELL JR., University, Va.

RECENT DEVELOPMENTS IN THE TREATMENT OF CHOREA MINOR. WALTER WHITAKER, Illinois M. J. **43**:123 (Feb.) 1933.

Whitaker reports that there seems to be no danger from the use of phenyl-ethyl-hydantoin in the treatment of children with properly controlled cases of chorea minor without evidences of existing complications. He believes that phenyl-ethyl-hydantoin offers a valuable aid in therapy, particularly in the more severe cases of chorea; by thus shortening the active stage of chorea, the incidence of subsequent carditis may be lessened.

BARBOUR, Peoria, Ill.

AMAUROTIC FAMILIAL IDIOCY. JULIUS F. MEYER, Illinois M. J. **43**:350 (April) 1933.

Meyer reviews the literature on amaurotic familial idiocy and reports two cases.

BARBOUR, Peoria, Ill.

THE LIPIDS OF THE BLOOD PLASMA IN EPILEPSY: I. A STATISTICAL STUDY OF SINGLE DETERMINATIONS IN 100 EPILEPTIC AND 32 "NORMAL" SUBJECTS. IRVINE MCQUARRIE, W. R. BLOOR, CLARA HUSTED and H. A. PATTERSON. J. Clin. Investigation **12**:247 (March) 1933.

The lecithin, cholesterol and fatty acid of the blood plasma were determined in a group of a hundred epileptic and thirty-two nonepileptic children under essentially the same conditions. No significant difference was found in the range of values for cholesterol or in its variability in the two groups. The mean value for lecithin was found to be significantly lower and that for total fatty acid significantly higher in the epileptic than in the nonepileptic subjects. The values for the phospholipin and the fatty acid showed significantly greater variability in the epileptic than in the nonepileptic subjects.

GUEST, Cincinnati.

THE LIPIDS OF THE BLOOD PLASMA IN EPILEPSY: II. VARIATIONS OF LIPIDS IN RELATION TO OCCURRENCE OF SEIZURES. IRVINE MCQUARRIE, CLARA HUSTED and W. R. BLOOR, J. Clin. Investigation **12**:255 (March) 1933.

Plasma lecithin, cholesterol and total fatty acids were determined repeatedly throughout the day in eight severely epileptic children. No constant relationship was found to exist between the absolute level of any of these constituents and the occurrence of seizures.

These lipid fractions were determined at different intervals in three other severely epileptic children under a variety of conditions. Hypercholesteremia and hyperlecithinemia were observed following the use of strongly ketogenic diets.

Whereas the absolute values for the individual lipid constituents of the plasma and those for the lecithin-cholesterol ratio differed greatly in the patients studied, there was a tendency for the ratio of lecithin to cholesterol to be higher at or near the time of convulsions than at other times.

GUEST, Cincinnati.

CLINICAL OBSERVATIONS ON THE VALUE OF THE HOFFMANN SIGN. TEMPLE FAY, J. Nerv. & Ment. Dis. **77**:394 (June) 1933.

This report is a study of 1,017 persons including 393 college students, 255 patients suffering from organic disease other than that of the nervous system and 339 patients suffering from organic nervous conditions. The Hoffmann reflex is best elicited by grasping the hand of the subject so that the ulnar portion of the palm rests in the examiner's hand, with the forearm in the midportion between pronation and supination and the fingers relaxed. The nail of the middle finger or ring finger is snapped with the examiner's thumb and index finger. Slight or no movement of the subject's thumb and index finger indicates that there is no organic disease above the midcervical region. In cases of disease above the fifth segment of the cervical portion of the cord there is a quick involuntary approximation of the thumb and the index finger, with simultaneous flexion of each in an approximating movement. It is comparable to the Babinski reflex in organic disease of the cortical spinal pathways.

JAHR, Omaha.

CHEMICAL STUDIES IN THE EPILEPTIC SYNDROME. HELEN HOPKINS, J. Nerv. & Ment. Dis. **77**:601 (June) 1933.

Since cholesterol has a definite influence on metabolic processes and since it bears a relationship to the acid-base equilibrium, water metabolism, cell permeability

and like factors, and in view of the ketogenic effect on epileptic attacks, there may be some relationship between the cholesterol content and epilepsy. Seven cases were studied, and 104 determinations of whole blood cholesterol were made at intervals of three hours throughout a twenty-four hour period. Generally figures are slightly lower in epileptic patients than in normal persons; however, the range of variation from hour to hour is greater in epileptic patients than in normal persons.

JAHR, Omaha.

TETANY IN YOUNG INFANTS. ABRAHAM S. SMALL, J. Pediat. **2**:681 (June) 1933.

A case of tetany beginning on the ninth day of life is reported. The serum calcium was 5.6 mg. per hundred cubic centimeters of blood. The Chvostek sign was negative. Blood found in the spinal fluid, obtained by lumbar puncture, was interpreted as being due to trauma. Recovery occurred rapidly following the administration of calcium chloride.

LEMASTER, Evanston, Ill.

MENINGITIS IN INFANTS AND CHILDREN WITH SPECIAL REFERENCE TO AGE-INCIDENCE AND BACTERIOLOGIC DIAGNOSIS. LEROY D. FOTHERGILL and LEWIS K. SWEET, J. Pediat. **2**:696 (June) 1933.

In 705 cases of meningitis in infants and children up to 12 years of age, the following types occurred: tuberculous, 290 cases; meningococcic, 160; influenzal, 78; hemolytic streptococcic, 69; pneumococcic, 69, and all other types, 39. The majority of cases of each type occurred during the first two years of life. Particularly emphasized are the incidence of influenzal meningitis and the value of chocolate agar as a culture medium for routine use with spinal fluid. The characteristic findings in the spinal fluid in each type of meningitis are briefly discussed.

LEMASTER, Evanston, Ill.

THE TREATMENT OF POLIOMYELITIS: PAST AND PRESENT. JOHN RUHRÄH, J. Pediat. **3**:217 (July) 1933.

The history of the treatment of the paralysis resulting from poliomyelitis is briefly discussed. The author stresses the point that the tendency is to recovery and that contractions and deformity can be prevented. Permanent paralysis is often due to neglect or improper management. The fundamental principles to be observed in treating the paralyses are outlined.

LEMASTER, Evanston, Ill.

CONFLICT OF CULTURES AND CHILDREN'S MALADJUSTMENT. JOHN LEVY, Ment. Hyg. **17**:41 (Jan.) 1933.

This article comprises a study of the case histories of children who present problems arising from the impact of two or more cultures on them. It aims to show how differences in language, manners, sexual training and ideals have affected them. Particular stress is laid on the child of foreign birth who was well enough adjusted in his original rôle, but who, through a change of environment, finds himself out of harmony with his surroundings. The author is of the opinion that the very proficiency with which the child has adapted himself to one cultural pattern unfits him for the new pattern that he is called on to adopt.

ABRAMSON, New York.

CHILDREN OF SCHIZOPHRENIC PARENTS. EDNA M. LAMPRON, Ment. Hyg. **17**:82 (Jan.) 1933.

In collaboration with the Rhode Island Society for Mental Hygiene, the author conducted a six months' follow-up study of the offspring of parents who had been committed to the Rhode Island State Hospital for Mental Diseases during the five

year period from January 1915 to January 1920. Complete data were obtained from 75 families in which one parent had been a patient at the hospital with a condition which had been diagnosed as schizophrenia; 80 per cent of the cases were of the paranoid type. Of the 75 matings, there were 244 offspring, of whom only 186 could be reached. Of this number, 98 were males and 88 were females. The investigation showed that in 38, or 50 per cent, of the families investigated there were from 1 to 4 children who were either mentally or socially maladjusted. Of the 186 offspring, 56, or 30 per cent, were maladjusted. Of the 56 who were maladjusted, 36, or 65 per cent, owed their condition to endogenous factors; i. e., 3 suffered from psychoses, 7 from mental deficiency and 7 from potential psychoses; 10 were emotionally unstable, 1 suffered from recurring depression, 2 were suicides, 4 were seclusive, and 2 were neurotic. The remaining 20 apparently owed their condition to exogenous factors; i. e., there were 7 wayward persons, 1 person in prison for murder and 12 who were worried about heredity but who were emotionally controlled.

ABRAMSON, New York.

SANITY IN MENTAL HYGIENE. A. MYERSON, Ment. Hyg. **17**:218 (April) 1933.

The author states that mental hygiene is a great humanitarian movement and that those who are in it have a great responsibility. They must not proclaim that they know what they do not know or can perform that which is at present impossible. They must not breed disillusionment, disgust and contempt. They must not, by inference, lead to the belief that every deviation from a hypothetic normal standard that a child or person shows is pathologic. Mental hygiene must not become propaganda. It must have the objectivity of science. It must carry on further research, the first step in which is to draw a clear distinction between what is known and what it is hoped will be known.

ABRAMSON, New York.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL; CASE 19231: STRABISMUS, HEADACHE AND OPISTHOTONOS. New England J. Med. **208**:1215 (June 8) 1933.

A boy, aged 4, was admitted to the hospital with strabismus, headache and opisthotonos supposed to be due to a fall down several steps, a month before admission, in which the forehead was struck. Details of the clinical history and laboratory and roentgen examinations are discussed. The preoperative diagnosis was cerebellar tumor. A tumor, 4.5 by 4 cm., completely filling the fourth ventricle, was found. The anatomic diagnosis was ependymal glioma (spongioblastoma) of the fourth ventricle.

GENGENBACH, Denver.

ENCEPHALITIS, POLIOENCEPHALITIS AND VACCINIAL ENCEPHALITIS IN CHILDREN. C. PAGET LEPAGE, Brit. M. J. **1**:811 (May 13) 1933.

An introductory discussion is offered as to the frequency, character, etiology and other features of encephalitis, and mention is made of some of the other infections of the brain. Vaccinal encephalitis is discussed with regard to frequency, location and morbidity and mortality and an outline of symptoms is given. The treatment suggested by the author for this condition is the intrathecal injection of serum from immune persons. Apparently good results have been obtained from this method of treatment. Next, polioencephalitis is discussed as to both etiology and symptomatology; again from 20 to 50 cc. of convalescent serum injected intrathecally has been employed in treating this disease. The serum is difficult to obtain. The symptoms and possible etiology of epidemic encephalitis (lethargica) are next described. Treatment consists in general measures. Belladonna and scopolamine are useful in the later stages and in sequelae, but they are not important in the acute stages. In the author's opinion, the serum of convalescents offers the best treatment for this condition. A brief mention is made of exanthematous encephalitis.

ROYSTER, University, Va.

TREATMENT OF SYDENHAM'S CHOREA. DONALD BATEMAN, Brit. M. J. **1**:1003 (June 10) 1933.

This is an outline of the author's experiences with the treatment of chorea by means of injections of typhoid vaccine, as done by Hendee Smith and Lucy Porter Sutton at Bellevue Hospital, New York.

ROYSTER, University, Va.

PARTIAL DEAFNESS SIMULATING CONGENITAL AUDITORY IMPERCEPTION. E. MILDRED CREAK, J. Neurol. & Psychopath. **13**:133 (Oct.) 1932.

This is the report of a case in a child, aged 8 years, who, though apparently neither deaf nor mentally defective, had no comprehension of ordinary speech. She had a language of her own which consisted of several noises and sounds. The previous history was apparently negative as far as other phases of development were concerned. She attended school and could copy letters, but she could not write to dictation or read. Yet her intelligence quotient was 95, and there was no trace of hysterical behavior. Vestibular tests and tests of the hearing gave negative results. A diagnosis of congenital auditory imperception was made. A comprehensive discussion of the literature and a valuable description of various tests of the hearing are included.

JAHR, Omaha.

THE SO-CALLED LAW OF ANTICIPATION IN MENTAL DISEASE. ARTHUR S. PATERSON, J. Neurol. & Psychopath. **13**:193 (Jan.) 1933.

The law of anticipation implies that a hereditary disease manifests itself in the offspring at an earlier age in each succeeding generation. The records of more than 4,000 were studied to test the law in its application to mental disease. The analysis of the cases does not bear out the correctness of the law in psychiatry.

JAHR, Omaha.

CEREBROMACULAR DEGENERATION. E. D. MACNAMARA, W. E. DIXON and R. T. HILL, J. Neurol. & Psychopath. **13**:211 (Jan.) 1933.

The case of a gentile boy, aged 6 years, who died of cerebromacular degeneration, is recorded. Macular changes were not prominent. The child was 3 years old at the onset of the condition, which progressed slowly with progressive loss of vision and hearing as well as mentality. The postmortem observations were generalized globose swelling throughout the brain and the cord, disappearance of Nissl granules and diminution of dendrites and progressive and widespread demyelinization of the white fibers of the cerebrum, including the optic nerve, cerebellum and brain stem.

JAHR, Omaha.

INFANTILE TRICHOTILLOMANIA. W. J. O'DONOVAN, Proc. Roy. Soc. Med. **26**:836 (May) 1933.

A case of trichotillomania is reported in a boy, aged 3 years. He would wet his fingers, pluck his hair out, examine it and then throw it away. The author wrote to the superintendent of the Zoological Society Gardens to inquire whether this habit is common among the higher apes. The reply is given in the report.

WILLIAMSON, New Orleans.

ACUTE MENINGITIS DUE TO DIPLOCOCCUS CRASSUS. J. COLUMBE and F. SAUVAGE, Arch. de méd. d. enf. **36**:420 (July) 1933.

Numerous observations have attested the rôle of Diplococcus crassus in the pathogenesis of meningitis, as well as in the etiology of various forms of septicemia, of pseudolobar pneumonia and of otitis media. This organism may act independently or may be associated in one of the aforementioned conditions with the

meningococcus of Weichselbaum or the tubercle bacillus. The authors report a case of meningitis in an infant, aged 2½ months, in which the causative factor proved to be Diplococcus crassus.

AMESSE, Denver.

AN EXTRAORDINARY CASE OF HYDROCEPHALUS. JOSUE A. BERUTI, Arch. med. d. hosp. Ramos Mejia **15**:77 (Sept.) 1932.

A mother, whose abdominal circumference measured 105.5 cm., was delivered of a 7 months' fetus. The head measured 80 cm. in circumference and contained 10 liters of fluid. The child's total weight was 9,750 Gm. Histologic sections showed this to be a primary form of hydrocephalus, that is, one not due to a tumor or to meningeal inflammation.

SANFORD, Chicago.

MEDICOPEDAGOGIC OBSERVATIONS ON CHILDREN. J. PORTELL VILA, Arch. de med. inf. **2**:61 (March) 1933.

The author establishes a gradual series of classifications to be applied in medicopedagogic observations on children chiefly of the school age. A synthetic description of the different kinds of attention is given, and the evolution of the spoken language in the child is discussed. The order to be observed in the clinical examination of abnormal children, with regard to the most frequent psychomotor disturbances, is described. This is an excellent article and should be read in full by any one interested in such matters.

SANFORD, Chicago.

COMPRESSION OF THE SPINAL CORD IN THE CHILD. D. ANTONIO LOSTRES GALLIFA, Med. de los niños **3**:288 (Oct.) 1932.

Medullary compression may be caused by (1) traumas, fractures of the vertebral column, luxations and hemorrhage; (2) infection, abscesses, Pott's disease and leptomeningitis or thrombophlebitis of the venous plexus in the spinal canal, and (3) neoplasms: extradural and intradural tumors, and tumors in the lumbar and sacral region, as well as spina bifida occulta.

The principal symptoms of compression of the cord are: pain, cold extremities, exaggerated reflexes, disturbances of sensibility or, in some cases, abolition of tactile sense, deep reflexes and flaccid paralysis. Xanthochromia and massive coagulation of the spinal fluid are characteristic signs of injury to the cord. The intraspinal injection of iodized poppy seed oil 40 per cent is of value in the differentiation by roentgenograms. By changing the position of the patient, first in the horizontal, then in the Trendelenburg position, the movement of the oil will help to localize the lesion. The contour of the shadow is also of value in making the differentiation between the various lesions; for example, the regular oval image indicates a benign tumor and the irregularly shaped shadow suggests a malignant process. The injection of air after the method of Cushing and Dandy is also described. The variations in the intraspinal fluid pressure, the Queckenstedt sign, made by pressure on the jugular veins are also of diagnostic value. Normally the initial pressure is 15; with mild compression, it is 20, and with severe compression, 60.

In the treatment, radiation should be used for compressions of neoplastic origin.

DWYER, Kansas City, Mo.

ASEPTIC MENINGITIS AND ENCEPHALITIS. RICHARD GROSSER, Monatschr. f. Kinderh. **57**:452, 1933.

The author has collected about thirty cases during the past few years in which the patients showed signs of meningitis or meningo-encephalitis, but in which the spinal fluid was sterile. These patients often showed isolated facial paralyses or even paralyses of the extremities. Some of the patients entered the hospital in a

state of coma. Some had disturbances of the optic nerve. In some instances the spinal fluid was at first perfectly clear, and then became purulent, but in all cases the cultures were negative. Practically all the patients recovered.

GERSTLEY, Chicago.

THE FUTURE OF CHILDREN WITH INTRACRANIAL HEMORRHAGE AT BIRTH. W. CATEL, Monatschr. f. Kinderh. **58**:89, 1933.

There is still disagreement as to whether the syndrome of Little's disease is due to injury and hemorrhage at birth or to a maldevelopment of the brain. Using the modern methods of obtaining bilirubin in the blood serum and in the spinal fluid as an index of cerebral hemorrhage, the authors studied thirty-nine children, most of whom were born prematurely.

In six of eight children who had no physical signs but positive laboratory findings, and in twelve of eighteen children who in addition showed physical signs, the mental and physical development was normal. In no child who showed definite laboratory and physical findings of intracranial hemorrhage were there symptoms of Little's disease, such as adductor spasm or spastic paraplegia.

The author considers that the syndrome of Little's disease is unquestionably one of cerebral maldevelopment.

The symptoms of intracranial hemorrhage fall into two groups: spastic hemiplegia and disturbances in the tone of skeletal musculature, usually atonia.

GERSTLEY, Chicago.

TETANIGENIC SUBSTANCES IN THE THYMUS AND THE URINE. H. M. SCHUMACHER, Ztschr. f. Kinderh. **54**:265, 1933.

This article is a critical reply to Nitscke on his "tetanigenic hormones in the thymus and the urine." The author maintains that it is not necessary to suppose additional hormones to explain certain phenomena which follow the injection of extracts of the glands and the urine into rabbits, since the chemical nature of the extract was not studied and the symptoms of tetany were not produced by implantation of the thymus. (See also Selzer, H.: *Ztschr. f. Kinderh.* **54**:421, 1933.)

SHELLING, Baltimore.

SYMPTOMATIC CHOREA MINOR AFTER POISONING BY CARBON MONOXIDE. D. BAUMLER, Ztschr. f. Kinderh. **54**:280, 1933.

Choreic symptoms developed in a girl of 11 years seven days after poisoning by carbon monoxide. The symptoms persisted for some time, but after seven months she was free from the dystonic manifestation except for a slight hypotonia.

SHELLING, Baltimore.

Diseases of the Eye

INDICATIONS FOR TREATMENT FOR COMBINED LATERAL AND VERTICAL STRABISMUS. JAMES WHITE, Arch. Ophth. **10**:585 (Nov.) 1933.

There has always been a discussion as to which imbalance should receive attention first in a combined lateral and vertical imbalance. To study the nature of an individual case White summarizes the steps in the examination:

"1. Determine the amount of the combined lateral and vertical deviation for distant and near vision and note whether the prism which corrects the vertical deviation lessens to any appreciable extent the lateral deviation and, if so, how much.

"2. Note the character and measure the absolute or relative convergence near point.

"3. At about 33 cm. measure the lateral and vertical deviation combined in the six cardinal fields, noting again the effect produced on the lateral deviation by the correction of the vertical deviation.

"4. Make excursion tests in the six cardinal positions with first one eye fixing, then the other. . . .

"5. Know the effect of an ametropic correction." WESCOTT, Chicago.

HEREDITY AND FAMILIAL KERATITIS: DEGENERATION AND OPACITY OF THE CORNEA. J. ROLLET, Arch. d'opht. **50**:161 (March) 1933.

The lesions included in this paper by Rollet have been described under the terms "keratitis," "degeneration" and "dystrophy," and may appear in an otherwise normal eye, at different periods of life. The cases are classified into those that are congenital and those that appear later in life. All the subdivisions are diagrammatically depicted.

The congenital group, which includes only two varieties, superficial and deep, have the following general characteristics: The lesions are visible from birth and change very little if at all. If any change does occur the condition tends to improve. The lesions are in the nature of remains or sequelae of an intra-uterine process. The condition is an anomaly of development found in several members of the same family. It is a permanent malformation in contrast to the progressive changes of the second group. Furthermore, the congenital lesions produce no functional or subjective symptoms other than lowered visual acuity in proportion to the degree of disturbance of transparency. Rollet gives case reports and pedigrees illustrating both the superficial and the deep varieties. The mode of transmission has not been demonstrated. The deep variety is illustrated by a family which he observed. In this instance the lesion had the appearance of a leukoma analogous to that seen after keratitis. Two theories based on study with a slit lamp are presented to explain the opacities: (1) that the elements of the corneal stroma have been irregularly laid down as in the sclera, and (2) that the stromal elements have not been sufficiently modified and contain substances which interfere with transparency.

The cases which appear later in life are of greater importance than the congenital cases. In contrast to that group, these lesions most often develop slowly and fatally; sometimes, as in the case of recurrent erosions, they regress and disappear spontaneously. When there is loss of epithelium the possibility of infection is added and makes the understanding of these cases more difficult. The first type of the superficial variety of this second group is represented by recurring ulcerative heredofamilial keratitis or recurrent erosion of the cornea. Franceschetti has shown in a recent report that recurrent erosions of the cornea may have a heredofamilial basis. In the case reported by this author the onset was at the age of from 4 to 6 years, the first attack having been brought on by an injury. Usually as the victims grow older the attacks diminish in frequency and severity. The cure may be complete or with a nebula. The anomaly acts as a dominant character, passes by direct transmission and is not propagated by those who are immune.

The second type of the superficial variety is a reticular superficial form. The term "reticular" was suggested by Koby, who has described the condition in detail. It occurs in middle-aged persons. Its development is extremely slow, without pain or inflammation, the patient having the sensation of a cloud before the eyes, vision gradually failing. The patient is otherwise healthy. It is bilateral, but to an unequal degree. The central portion of the cornea presents a faint opalescent appearance, limited above, as a rule, by a superficial line, like a thread of mucus. It has three characteristics under biomicroscopic examination, which are (1) zones of bedewing of the epithelium with fine opacities, (2) crevices in Bowman's membrane and (3) an epithelial line in relief. According to Koby, the lesion is situated in the neighborhood of Bowman's membrane.

The third type of this subdivision is the speckled. The author presents the pedigree of a case which he had previously reported as belonging to the reticular

type described by Koby. In this condition the onset occurs between the ages of 9 and 12. Gradual failure of vision occurs, accompanied by pain, itching, congestion and tearing. The center of the cornea is especially vulnerable, and with the naked eye a large number of whitish superficial spots are seen. With the biomicroscope an irregularity of the cornea is seen. In optical section the lesion is seen to be situated in front of Bowman's membrane, which is normal.

The second group of late-appearing heredofamilial conditions is that of the interstitial or deep varieties. These are especially slow in development and are in the nature of a degeneration or a dystrophy. They may appear soon after birth, during childhood or adolescence, or even at an adult age. The lesions involve the stroma of the cornea.

The first three types are fairly well demarcated. These are the nodular, the speckled and the neuro-edematous. The fourth or plexiform type is not so clearly defined. In it there may or may not be specks, nodules and striae. Its polymorphous nature is such that its subsequent course alone determines the diagnosis.

The nodular type is the nodular keratitis first described by Groenow in 1890. Some doubt was entertained as to whether this is a dystrophy until Koby's recent careful report. Failure of vision takes place slowly. There are few symptoms. Its onset is in adolescence. Nodules of a hyaline, whitish, yellowish or grayish color are seen in the cornea and produce elevations on its surface, depending on their location. Its course is slow.

The speckled type is that which Fehr and Hambresin have carefully described. The author presents the pedigree in a personal case. White specks are seen in the center of the cornea which appear as plates in the stroma and never raise the corneal surface. The cornea maintains its transparency; the nerve fibers remain normal and are unrelated to the specks. Sensation is normal. Slow progressive changes take place, resulting in partial blindness.

The neuro-edematous type consists in a change in the nerve fibers best seen with the biomicroscope. The onset is slow, with intermittent attacks of pain, photophobia, congestion and tearing. Radiating striae are seen in the middle third of the cornea, with a distribution and branching characteristic of nerve fibers about five times their thickness. These striae are made up of fine granules, no fibrillae being visible. Although the cornea remains normal for a long time, ulceration is liable to occur. Folds in Descemet's membrane may be seen as the disturbance progresses, and in old cases the corneal opacities sometimes have the appearance of calcified deposits. This form of degeneration occurs in adults.

The plexiform type of interstitial degeneration occurs in a variable form made up of specks and striae. It throws doubt on the classification of these hereditary corneal lesions, for the lesions may appear as though they were stages of transition from one form to another.

The latter part of this extensive contribution is devoted to the discussion of the pathology, etiology, diagnosis, prognosis and treatment of the various conditions.

S. B. MARLOW. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

SINUSITIS IN CHILDREN. HENRY A. REISMAN, Arch. Pediat. **50**:795 (Nov.) 1933.

The general subject of sinusitis in children is discussed, and attention is particularly called to the enlargement of the submaxillary glands as an aid to early diagnosis.

WADDELL JR., University, Va.

SPEECH DISORDERS OF PHYSICAL ORIGIN. JOHN A. GLASSBURY, Arch. Pediat. **50**:802 (Nov.) 1933.

The writer Glassbury believes that treatment of disorders of speech is peculiarly a medical problem, and classifies and discusses some of the common disturbances

of speech. He would classify stammering as a neurosis of speech coordination based on a mental conflict—a definite pathologic condition. He thinks that defective formation of words, with the exception of a foreign accent and improper pronunciation, should be considered as based on physical and often remedial causes.

WADDELL JR., University, Va.

BLOOD INFECTION FROM OTITIS MEDIA: ANALYSIS OF SIXTY-THREE CASES. E. J. G. GLASS, J. Laryng. & Otol. **48**:754 (Nov.) 1933.

An analysis of sixty-three cases of infection of the blood from otitis media is presented by Glass. The patients are divided into groups, and the comparative mortality rates are given. The following groups have a relatively low mortality rate: (1) children under 10 years of age, (2) persons with otitis media operated on during the first week, (3) persons in whom metastatic abscesses develop and (4) persons with hemolytic streptococcic infections treated with antiscarlet fever serum. The prognosis is bad: (1) in patients over 40 years of age, (2) in patients with chronic suppurative otitis media with acute exacerbation, (3) if septicemia has developed before operation and (4) in patients showing subcutaneous hemorrhage or jaundice.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TUBERCULOSIS OF THE EAR. DOUGLAS GUTHRIE, Tr. Edinburgh Med.-Chir. Soc., 1933, p. 169; in Edinburgh M. J., Sept., 1933.

Guthrie stated that tuberculosis of the ear has become much rarer within the past ten years. This form of suppuration of the middle ear is usually gradual and painless in development; the surrounding lymph glands are much enlarged. In about 50 per cent of the cases there is facial paralysis. A complete mastoidectomy must be done if one is to eradicate the disease. The general condition of the patient at this time determines the prognosis, which is not always hopeless. Guthrie showed a boy, aged 13 years, who had been operated on at the age of 5 months.

Dr. C. E. Scott presented a case in an infant, 7 months old, which might be mistaken for one of tuberculosis of the ear. The auricular glands were enlarged, softened and broken down, and there was facial paralysis, but the pus and granulations had shown Bacillus influenzae. A 2 year old child was presented, showing the healing stage after an operation for tuberculous mastoiditis. Logan Turner was reported to have said that suppuration of the middle ear in infants under 1 year of age is tuberculous in 50 per cent of the cases and possibly due to infective milk.

NEFF, Kansas City, Mo.

A CASE OF NASOPHARYNGEAL TORTICOLLIS. J. GUÉRARD, R. POTVIN and J. B. JOBIN, Bull. Soc. méd. d. hôp. universitaires de Québec **34**:58 (Feb.) 1933.

A girl, aged 9 years, came to the hospital, complaining of a red and painful swelling which had appeared two days before in the left nasal ala and had spread rapidly to the left eyelid and then to the entire left side of the face. The temperature rose to 104 and 105 F.; the pulse was feeble, and the patient was stuporous. A few days later the upper eyelid on the left side suppurated and was incised, after which the skin of the entire lid sloughed away. Soon the left side of the scalp and face began to suppurate profusely and became denuded of skin. The septicemia lasted eight months, with slow improvement. During this period osteo-arthritis of a finger of the right hand occurred, with extensive osteoperiostitis of the right femur, osteitis of the right humerus, an abscess of the left lung and a renal complication the presence of which was revealed by pyuria and hematuria. An unusual complication consisted in an inability to rotate the head, which developed during several days and which was characterized by fixity of the head and neck, with massive cellulitis in the latter region, all depending on rotation of the atlas by which one side, usually the left, projected forward beyond the

other, and on a cervical curvature of the spine, with the convexity to the right. In this right-sided protrusion could be felt the spinous process of the axis, pushed to the right by the sliding forward of the axis and its rotation to the left. This was brought out by roentgenograms. The condition was diagnosed as nasopharyngeal torticollis. This disease was first described by P. Grisel in 1930 and has received the name of Grisel's disease. It occurs chiefly in girls from 8 to 12 years of age, following the appearance of an abscess in the retropharyngeal region or other angina of the throat. If it is not recognized and treated, it becomes chronic. In this stage a characteristic sign is the "sternal paradox," meaning that the sternocleidomastoid muscle which contracts tonically is that not of the affected but of the opposite side.

VINTON, Brooklyn.

TRACHEOBRONCHIAL CROUP, PROBABLY STREPTOCOCCIC; CURE BY TRACHEOTOMY AND BRONCHOSCOPY. CAYLA, BUNEAU and WILM, Bull. Soc. de pédiat. de Paris **30**:681 (Dec. 20) 1932.

A boy, 6 years old, who had been immunized against diphtheria two years previously, had laryngitis and tracheobronchitis. He was on the point of suffocation when intubation was tried; the boy stopped breathing and became markedly cyanosed, so that immediate tracheotomy was done. After five minutes of artificial respiration and administration of oxygen he recovered. The following day he had marked dyspnea which was not relieved by cleaning of the tracheal cannula and removing as much membrane as was possible through the tracheotomy opening, so a bronchoscope was inserted and by means of forceps the trachea was cleaned of all membrane as far as the bifurcation. The child improved, and the tracheal tube was removed four days later without subsequent trouble. No diphtheria bacilli were grown in repeated cultures made from the membrane, but a pure growth of streptococci was obtained. Repeated doses of diphtheria antitoxin were administered, even though the child had been ill for six days when he was admitted to the hospital and despite cultures negative for Bacillus diphtheriae. When membrane extends beyond the larynx, bronchoscopy is indicated.

BENJAMIN, Montreal, Canada.

A STUDY OF THE ALLERGIC CUTANEOUS REACTIONS IN INFANTILE ECZEMA. S. NOGUER MORÉ, Paidoterapia **12**:559 (Oct.) 1933.

The mechanism of so-called infantile eczema was studied in sensitization tests. These tests proved that eczema may be present independent of exogenous agents (alimentary substances, etc.) which normally produce sensitivity. The marked frequency of hypersensitivity without previous sensitization leads one to admit that allergy due to a constitutional predisposition (Debre) is a causative factor. Hypersensitivity to the usual germs in the intestinal tract permitted demonstration of the "isomorphous effect of Kubner" in six of thirty-two cases. Hypersensitivity to egg-white, injected intradermally, was investigated in thirty-two children, twenty-four of whom had never before taken this food; 9 per cent gave strong positive, and 14 per cent weak positive, reactions. The cutaneous reactions, except in a few cases, were urticariform. In three of sixty cases true eczema was reproduced by the tests.

The sensitization in infantile eczema is very complex, multiple antigens being the cause, producing polyvalent allergy which, in turn, shows no close reaction to the antigen that started it. The identification of the antigen is difficult if not impossible.

Desensitization was tried with 10 per cent solutions of albumin, starting with 0.1 cc. and increasing to doses of from 1 to 2 cc. These injections were followed by a diminution in the lesions, but they did not produce immunity. Albumin acts as an antigen and is of value in desensitizing the patient.

HERRON, Spokane, Wash.

TONSILLAR FUNCTION AND SURGICAL THERAPY OF THE PALATINE TONSILS. GIUSEPPE SALVADORI, Méd. inf. **2**:45 (Feb.) 1933.

One school holds that the tonsil is a lymphatic organ possessing a hematopoietic function, and that its functions are closely related to, and intimately associated with, those of the spleen, thymus, bone marrow and lymphatic glands. Another school believes that it produces lymphocytes only as a defensive organ reacting to exogenous and endogenous stimuli. A third is of the belief that the tonsil represents a residual embryonic organ, harmful to the organism in that it serves as a portal of entrance for various infections, and that it should always be removed.

Marfan concludes after an exhaustive review of the literature that the tonsils are useful organs either because of their hematopoietic function or because they serve as a front line defense against external causes of morbidity. However, when they become the seat of pathologic processes, they become harmful and should be removed, as their absence is compensated for by numerous other organs with analogous functions.

COPPOLINO, Philadelphia.

INTRABRONCHIAL INJECTION OF IODIZED POPPY SEED OIL 40 PER CENT, USING A MODIFICATION OF THE TECHNIC OF GARCIA CAPURRO. PEDRO CANTONNET, JOSÉ A. SOTO and HECTOR CANTONNET, Arch. de pediat. d. Uruguay **4**:163 (May) 1933.

The authors describe a technic of bronchography in which iodized poppy seed oil 40 per cent is used as a contrast medium. Thorough anesthetization of the bronchial mucous membrane is necessary. Their modification of Garcia Capurro's technic, particularly of the instruments used, makes the procedure simple in fairly skilled hands.

SCHLUTZ, Chicago.

TREATMENT OF MASTOIDITIS. MAX MEYER, Jahrb. f. Kinderh. **138**:114 (Jan.) 1933.

This article is a vigorous polemic against Zischinsky, who advised expectant treatment in mastoiditis and otitis media complicating infectious diseases (*Jahrb. f. Kinderh.* **136**:310, 1932).

CLAUSEN, Rochester, N. Y.

TREATMENT OF MASTOIDITIS. V. HINSBERG, Jahrb. f. Kinderh. **138**:233 (Feb.) 1933.

This article is a reply by an otologist to Zischinsky, who advocated expectant treatment for mastoiditis secondary to contagious diseases (*Jahrb. f. Kinderh.* **136**:310, 1932).

CLAUSEN, Rochester, N. Y.

THE PROBLEM OF THE TONSILS. T. J. BÜRGERS and W. WOLFFHEIM, Klin. Wchnschr. **10**:1064 (June 6) 1931.

An attempt was made to associate pathogenic bacteria obtained from the tonsils with the pathologic processes in those structures. Use was made of the percentile index (Fresszahl), or the proportion of leukocytes taking part in phagocytosis. It was found that in infection of the tonsils the index was low, suggesting low defensive powers, and that following tonsillectomy the index rose to 50 per cent or more. In cases in which the index was originally around 50 per cent, the authors believed that the tonsils could not be incriminated or that the defensive mechanism was sufficient to take care of the infection without surgical intervention; further observation is called for, however, because this relationship could readily change.

SILVERMAN, Syracuse, N. Y.

ANATOMY AND GENESIS OF CONGENITAL ATRESIA OF THE EAR. F. ALTMANN, Monatschr. f. Ohrenh. **67**:765 (July); 917 (Aug.); 1042 (Sept.) 1933.

Altmann discusses congenital auditory atresia on the basis of a study of the serial microscopic sections and wax models from eight cases (thirteen temporal bones) and the valid cases found in medical literature. The structure often differs in individual cases. The term congenital atresia of the ear does not designate a single well characterized malformation but a whole complex of generally causally syngenetic malformations (owing their development to the same cause) associated in various combinations. They concern the posterior portions of the two superior visceral arches and involve the structures of the middle ear in varying degrees. The cause of the development of this complex must be an injurious factor the influence of which has affected the whole anlage of the ear, particularly in the region of the external and middle ear. The author divides the malformation into three genetically similar groups according to their severity. In the first group a tympanic ring (even if poorly developed) and a rudimentary tympanic membrane exist. The tympanum exhibits only slight changes. The second group exhibits great polymorphism. The tympanic membrane is severely malformed or lacking, and the tympanum is usually diminished in size. There are two subdivisions, depending on the presence or absence of the tympanic membrane. Proliferation of parts of the second visceral arch (stylohyoid or tympanohyoid or a combination) can occur in both. In the absence of a tympanic membrane and with slight or no hyperplasia of the second visceral arch there is development of the squama temporalis and the floor of the tympanum, which reduces the defect. This development appears to be in inverse proportion to the proliferation of the second visceral arch. The third group comprises the most severe cases, in which a tympanum did not develop. This classification considers only the condition of the middle ear, but a certain parallelism between the degree of malformation of the latter and that of other parts of the ear exists. The termination of the teratogenic period is usually a stage of development in which the embryo is from 16 to 20 mm. in length. In the severe forms, however, it may often be an earlier period.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

RECOGNITION OF CHRONIC TONSILLITIS. W. KRAINZ and F. J. LANG, Monatschr. f. Ohrenh. **67**:1096 (Sept.) 1933.

In an extensive investigation for the purpose of finding an objective clinical sign of chronic tonsillitis which would be demonstrable in all cases of this disease, Krainz and Lang found that in all cases there are sensitivity to pressure in the tonsillar fossae and palpable hardening of the posterior side on palpation of the fossae from the exterior. Histologic examination of fifty tonsils in such cases disclosed, in addition to the well known picture of chronic inflammation of the lymphatic tissue and the crypts, thickening, cicatrization and induration of the capsule and trabeculae of the connective tissue, thickening of the vascular walls and an accumulation of plasma cells and other inflammatory cells between the fibers of the capsule and the trabeculae and around the blood vessels and nerves, as well as around bundles of muscles. Comparative examination of tonsils which did not exhibit sensitivity to pressure in the fossae showed less cellular infiltration and absence of extensive cicatricial formations in the capsule and musculature. The objective clinical sign thus appears to be explained by the inflammation within the capsule and the muscle. These conditions are to be interpreted as the result of inflammation extending beyond the boundary of the tonsil. Despite the cicatricial contraction of the capsule, the muscular function is preserved. The objective sign here described is the major clinical sign in the recognition of chronic tonsillitis.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

THE RELATION OF MALOCCLUSION TO THE FORMATION OF THE SIBILANTS. LEO BARCZINSKI, Ztschr. f. Stomatol. **30**:1329, 1932.

Barczinski reviews the incidence of malocclusion in cases of sigmatism as reported by others. The figures given range about 75 per cent. In his study he undertook to determine the incidence of sigmatism in cases of malocclusion rather than to determine the incidence of malocclusion in cases of sigmatism, which is the usual procedure. Excluding those cases of sigmatism due to impaired hearing, defective intelligence and loss of the milk teeth, he found a ratio of thirty lispers to one hundred with anomalies of occlusion. Of these anomalies of occlusion the frontal open-bite malocclusion accounted for the greatest number of cases of lisping, a ratio of sixty to one hundred. As to the cause, he believes that the factors leading to the malocclusion could be genetically coordinated with those leading to the faulty function of the tongue. He found rickets in many cases to explain the malocclusion, and postulated that the disproportionate size of the tongue in relation to the crowded upper jaw interfered with the normal function of the tongue in producing the sibilants.

WOLF, Paterson, N. J.

SPEECH DEFECT: GENERAL CLASSIFICATION; ASSOCIATIVE APHASIA. ALEXANDRA STEPOWSKA, Pedjatrja polska **12**:485, 1932.

Speech defects are due to pathologic conditions. These conditions can be systemic, local or functional. The speech reflex as described by Lichtheime and Wernicki is as follows: The sounds are received by the hearing apparatus and transmitted to the Wernicki center, where sounds are recorded and impressed; understanding of speech, association of objects and remembrance of words and their significance become located in the transcortex; from there the impulse is transmitted to the Broca center, then to the nucleus of the motor nerves located in the fourth ventricle, pons Varolii and rhomboid fossa, and then to the nerves supplying the tongue, lips, palate and posterior part of the throat. This scheme is often questioned by new investigators. Speech defects are classified, according to the Vienna schools, as follows:

A. Dumbness: (*a*) surdo mutitos, or state of being deaf and dumb; (*b*) mutitos idiotatica, and (*c*) mutitos imbecillitatis

B. Aphasia (loss of speech previously present)

C. Dyslalia (defect in pronunciation of certain sounds)

D. Associative aphasia such as stammering, stuttering and faltering

E. Systemic speech defect, as in disseminated sclerosis, bulbar paralysis and chorea

F. Speech defect in mental disorders.

KRUPINSKI, Chicago.

ROENTGEN TREATMENT OF CHRONIC TONSILLITIS. ERIK WOLFF, Finska läk.-sallsk. handl. **75**:965 (Oct.) 1933.

Pathologic studies of tonsils subjected to roentgen radiation did not show atrophy or other marked changes. No bacteriologic studies were made.

ELGHAMMER, Chicago.

DEAF AND NONSPEAKING CHILDREN. H. BURGER, Maandschr. v. kindergeneesk. **2**:379 (May) 1933.

Deaf and dumb children of normal intelligence should attend a school for the deaf and dumb, by preference a day-school. If possible, they should enter a preparatory class of the school when they are 3 years old. Children who hear and speak and who become totally deaf before the seventh year should attend a school for deaf and dumb children as soon as possible, in order to prevent loss of speech. Deaf and dumb children with weak mentality should not attend a

school for mentally defective children, nor should they attend the ordinary class of the school for the deaf and dumb. It would be best to place them in a separate class in an institution for the deaf and dumb and to give them an education in which the dumb show is used. Deaf children aged 3 years with doubtful mental ability should be sent provisionally to a preparatory class of a school for the deaf and dumb. Dumb children 4 years of age and older with hearing and with normal mental abilities should be temporarily placed in a school for the deaf and dumb. If, after one or two years, they have learned to speak, they should attend the common school. Children who only hear poorly and who cannot follow the common school routine should attend a special school for children with deficient hearing.

VAN CREVELD, Amsterdam, the Netherlands.

Diseases of the Skin

LUPUS ERYTHEMATOSUS BEFORE PUBERTY. D. TRUETT GANDY, Arch. Pediat. **50**:652 (Sept.) 1933.

Two cases of lupus erythematosus occurring in early life are reported. Gandy believes this condition to be less rare than is usually supposed.

WADDELL JR., University, Va.

ACRODYNIA, A VITAMIN DEFICIENCY DISEASE. S. J. MCCLENDON, Arch. Pediat. **50**:666 (Sept.) 1933.

Two cases of acrodynia are reported which showed prompt improvement following the use of vitamin B therapy. The infants were given a diet rich in vitamin B, reenforced with haliver oil, vitavose, brewers' yeast and viosterol.

WADDELL JR., University, Va.

ASSOCIATED FACIAL AND INTRACRANIAL HAEMANGIOMATA. LAMBERT ROGERS, Brit. J. Surg. **21**:229 (Oct.) 1933.

Rogers reports a case of extensive extradural and intradural plexiform arteriovenous anastomoses connected with each other and associated with a facial capillary hemangioma (nevus) on the same side. The entity has been recognized for some time. Clinically there may be convulsions immediately followed by transient attacks of hemiplegia. As a rule there is little or no general progression of the signs and symptoms. Calcification may or may not be present.

There are definite indications that the condition should be treated, as there is always the danger of fatal intracranial hemorrhage, and the seizures are often alleviated. Rogers advocates osteoplastic exploratory craniotomy with occlusion of the principal source of blood supply to the lesion. The nature of the lesion is also discussed.

SUMMERFELDT, Toronto, Canada.

INFANTILE DERMATITIS. H. L. WALLACE, Tr. Med.-Chir. Soc. Edinburgh, 1933, p. 166; in Edinburgh M. J., Sept., 1933.

Six members of the immediate family of an infant, aged 9 months, with eczema suffered from some allergic disturbance. The diet was studied, and sugar, especially cane sugar, was found to be a chief factor in producing and maintaining the facial dermatitis which the infant had. The treatment is thereby suggested.

NEFF, Kansas City, Mo.

A CASE OF PIGMENTARY URTICARIA. G. BOULANGER-PILET, Bull. Soc. de pédiat. de Paris **30**:107 (Feb. 16) 1932.

A male infant, 9 months old, presented a maculopapular generalized eruption which had been present since the age of 3 months. The lesions were reddish and

varied in size from that of a pinhead to that of a lentil. In certain of these cases, which are not very common, the blood findings resemble those for leukemia, but such findings were not present in this instance.

BENJAMIN, Montreal, Canada.

FAMILIAL NEUROFIBROMATOSIS. L. BABONNEIX and RIOM, Bull. Soc. de pédiat. de Paris **30**:156 (March 15) 1932.

Left-sided hemiplegia involving also the lower part of the left side of the face had gradually developed in a girl 12 years old. She showed some brownish pigmented spots on the right flank and the internal surface of the right thigh. The father was afflicted with neurofibromatosis.

BENJAMIN, Montreal, Canada.

RECKLINGHAUSEN'S DISEASE — PIGMENTARY FORM, WITHOUT TUMORS. H. GRENET, P. ISAAC-GEORGES and L. LOUVET, Bull. Soc. de pédiat. de Paris **30**:536 (Nov. 15) 1932.

A boy, 10 years old, was presented, with a condition diagnosed as Recklinghausen's disease. He had no dermal or nerve tumors but showed numerous areas of light brown pigmentation on the trunk. He also had many deformities of the bones.

BENJAMIN, Montreal, Canada.

TWO CASES OF ACRODYNIA; TREATMENT WITH ACETYLCHOLINE. HENRI JANET, PIERRE VALLERY-RADOT and S. HUGUET, Bull. Soc. de pédiat. de Paris **30**:644 (Dec. 20) 1932.

Two severe cases of acrodynia occurring in a boy and a girl, each 3 years old, are reported. After they had shown very little, if any, improvement for about a month despite ultraviolet irradiation, they were given six injections of acetylcholine in doses of from 2 to 5 cg. at intervals of two days. The children rested better and showed some abatement of the symptoms after this treatment, but the redness and puffiness of the hands and feet did not change. Both of the patients began to show evidence of the disease in August; in a number of other cases the onset was during the winter and spring months, and it is therefore concluded that the disease is not a seasonal one, as has sometimes been asserted.

BENJAMIN, Montreal, Canada.

BERLOCQUE-DERMATITIS. FRIEDRICH ECKARDT, Monatschr. f. Kinderh. **59**:93, 1933.

This is a report with a photograph of a child with dermatitis of the chest. The appearance was that of irregular stripes, as if several drops of water had coursed down. The disease is one of those rare combination reactions in which the skin has first been sensitized by a certain drug and then exposed to sunlight. This case is one of a number of such. In this one cologne water (4711) had been applied to the skin and sixteen days later the infant was taken out and exposed to hot sunshine. Several such cases have been reported following the use of cologne water.

GERSTLEY, Chicago.

ERYTHEMA NODOSUM AND TUBERCULIN REACTIONS. EINAR GAMSTEDT, Monatschr. f. Kinderh. **59**:111, 1933.

Gamstedt reports the results of seventy-five tuberculin tests done on fifty-one persons with erythema nodosum just before or during the stage of eruption. Before the eruption fever all the reactions were negative. After the fever, however, all

were positive with one exception, and this one became positive on the fifth day. These observations suggest that the eruption fever is a sign of beginning allergy.

GERSTLEY, Chicago.

Surgery and Orthopedics

OSTEOMYELITIS. J. CHRISTOPHER O'DAY, Northwest Med. **32**:158 (April) 1933.

O'Day stresses the importance of early opening of the medullary canal in osteomyelitis; he recommends removal of a section of cortex ½ by 2 inches (1.2 by 2.5 cm.), avoiding trauma to the marrow contents. He cautions against confusion of diagnosis with rheumatism and also against relying too confidently on negative roentgenologic findings in excluding osteomyelitis.

SCOTT, Philadelphia.

THE TREATMENT OF TUBERCULOUS DISEASE OF THE HIP JOINT. A. S. BLUNDELL BANKART, Brit. J. Surg. **20**:551 (April) 1933.

The author believes that the experience of the past twenty-five years has proved that the so-called conservative treatment of tuberculosis of the hip joint has been a failure. In tracing the course of the disease in relationship to the pathologic process, he believes that the cavity can heal only by collapse or bringing together of the adjacent bones so that the tuberculous material is squeezed out and solid bone comes in contact with solid bone. Here also anything which prevents collapse of the bones and obliteration of the cavity will lead to the establishment of a chronic tuberculous cavity which may become encapsulated and though quiescent for years will remain unhealed and a constant menace to the patient.

There are reports of nine cases of radical operation and complete removal of the local disease. The after-treatment of the arthrodesis is to get the patient up early, that is, before the artificial fusion could possibly be strong enough to prevent ascent of the femur under the stress of weight-bearing. As a rule the patients were up and walking in from five to eight weeks after operation. All the patients now have stable, painless hips and, with one exception, at least some degree of useful movement.

SUMMERFELDT, Toronto, Canada.

ACUTE INFECTIVE OSTEOMYELITIS: A REVIEW OF 262 CASES. L. N. PYRAH and A. B. PAIN, Brit. J. Surg. **20**:590 (April) 1933.

This study covers a period of ten years. There were twice as many boys as girls, and the majority of the patients were between 5 and 14 years old. In this series, the most common site of acute osteomyelitis was at the upper end of the tibia and the lower end of the femur. This might be explained by the fact of the frequency of trauma at the knee joint and by the fact that there is a good metaphyseal blood supply. Trauma was found to be a predisposing cause in a high proportion of the cases. Other predisposing causes are septic finger, boils and impetigo. In about 90 per cent of the cases, Staphylococcus aureus was the causative organism. Autopsies were done in 51 cases, and in all except 6, pyemic lesions were found throughout the body, the most common complaint being pericarditis. The authors also discuss the symptomatology, treatment and results.

In this series 64 patients were treated by primary incision with a mortality rate of 25 per cent. The authors have had better results with this form of treatment than with the gutter operation. The gutter operation was performed in 176 cases, most of which were of average severity. The mortality rate was 29.5 per cent. A few patients were treated by the method of Winnett Orr, but the authors would not advocate its use. In summing up the results, they advocate the more conservative treatment of the disease.

SUMMERFELDT, Toronto, Canada.

TREATMENT OF ACUTE EMPYEMA IN INFANCY AND CHILDHOOD. J. D. McEACHERN, Brit. J. Surg. **20**:653 (April) 1933.

The author describes and gives the results in seventy-five cases of empyema in which the patients were treated by means of closed drainage. When the organism present is the pneumococcus, thick pus must be present for at least a week before drainage is attempted. In case of a streptococcic infection, thick pus must be present for at least ten days. McEachern also stresses the importance of preventing the entry of air into the chest during aspiration, as it causes spread of the infection and forms an additional menace to the life of the child. A clear and full description of the apparatus and of the technic of the operation is given, with a method of irrigation of the pleural cavity.

The results are very gratifying. Mortality rates of from 22.2 to 37.8 per cent in cases of empyema have been reported from various centers. In this series of patients treated with closed drainage, the author has had two deaths, both in children under 2 years of age. In seven cases there were bronchial fistulas which healed in from three to seven days after drainage was started. The average number of days of drainage was twenty-one and four-fifths, and there were no instances of chronic empyema. This is a much shorter time than is required by the open method, which is of economic value.

SUMMERFELDT, Toronto, Canada.

APPENDICITIS AND MECKEL'S DIVERTICULUM. G. A. WEIR, Brit. M. J. **1**:1053 (June 17) 1933.

This article is the report of a case which was diagnosed as appendicitis but which proved to be diverticulitis.

ROYSTER, University, Va.

SPINAL ANESTHESIA IN AN INFANT. I. D. KITCHIN, Brit. M. J. **2**:103 (July 15) 1933.

The author reports a case of intussusception in a child, aged 27 weeks, who was operated on under spinal anesthesia. The technic consisted in withdrawing a small amount of spinal fluid and in injecting intrathecally 3.5 cm. of a 5 per cent solution of benzoyl-dimethyl-amino-ethylpropanol hydrochloride and dextrose mixed with an approximately equal quantity of cerebrospinal fluid. The result was satisfactory in every respect.

ROYSTER, University, Va.

TREATMENT OF CYSTIC HYGROMA OF THE NECK BY SODIUM MORRHUATE. GORDON HARROWER, Brit. M. J. **2**:148 (July 22) 1933.

The author, who writes from the Medical College at Singapore, states that cystic hygroma is common in that section. He reports the case of a patient who was treated with an injection of a solution of sodium morrhuate, which acts as a sclerosing agent. The patient was apparently cured in a short time.

ROYSTER, University, Va.

JUXTA-ARTICULAR OILOMA OF THE HIP. RAPHAEL MASSART, Bull. Soc. de pédiat. de Paris **30**:116 (Feb. 16) 1932.

A boy, 4 years old, had pain in the right hip which caused him to walk with a decided limp. A tender swelling could be palpated at the side of the right hip joint. Roentgenologic examination showed a dense central area, resembling an injection of iodized poppy seed oil, with a surrounding area of lesser density corresponding to the swelling which was palpable; the entire shadow lay outside of the hip joint. It developed that the child had been given injections of mercurial oil and bismuth at the age of 16 months on the strength of a history of two miscarriages by the mother when she was married to her first husband; this child was the first offspring by her second husband. The seriousness of the condition

of oiloma, probably paraffinoma in this case, is emphasized, and a plea is made against the indiscriminate injection of antisyphilitic substances to patients in whom the presence of congenital syphilis is suspected on entirely inadequate evidence.

BENJAMIN, Montreal, Canada.

A CASE OF SCHLATTER-OSGOOD'S DISEASE. M. LANCE, Bull. Soc. de pédiat. de Paris **30**:628 (Dec. 20) 1932.

A boy, aged 14, showed hypertrophic epiphysitis of the tibial tubercles. He had suffered intermittent pain locally for three years. Roentgenologic examination showed some thickening of the tibial tubercles, which were ossified, with cuplike excavations in the anterior parts, giving the appearance of sequestra. There was no history of trauma. Ordinarily putting the limbs at rest in plaster casts for three or four months suffices to cure the condition; in the more refractory cases, however, it sometimes becomes necessary to operate.

BENJAMIN, Montreal, Canada.

EPIPHYSITIDES DURING THE PERIOD OF GROWTH. J. COMBY, Bull. Soc. de pédiat. de Paris **30**:630 (Dec. 20) 1932.

Referring to a previous meeting of the *Société* at which a case of so-called Schlatter's disease was presented, Comby points out that if any proper name is to be attached to this disease it should be that of Lannelongue, who described cases of it in 1878. Four cases are summarized which Comby reported in 1903, and which he had observed as early as 1889.

BENJAMIN, Montreal, Canada.

ANTERIOR TIBIAL EPIPHYSITIS, OR LANNELONGUE-SCHLATTER-OSGOOD'S DISEASE. M. OMBRÉDANNE, Bull. Soc. de pédiat. de Paris **30**:633 (Dec. 20) 1932.

This condition is fairly frequent. The lesion is associated with a dipping down of the anterior part of the superior metaphysis of the tibia, and this supports the tibial tubercle. The roentgenologic findings are similar to those in the so-called osseous dystrophies of adolescence. Trauma may play a part in the genesis of the condition, as it favors a separation of the epiphysis. Surgical intervention need be resorted to only in the rare instances in which excessive pain on walking persists. In such cases the part of the metaphyseal cartilage which is subjacent to the tibial tubercle should be removed with the latter; otherwise a painful swelling may recur at the site of the tubercle.

BENJAMIN, Montreal, Canada.

RECURRENT INTUSSUSCEPTION. ANDRÉ MARTIN, Bull. Soc. de pédiat. de Paris **30**:641 (Dec. 20) 1932.

A boy had an intussusception at the age of 3, a second one three years later and a third one when he was 8 years old. Operation was followed by recovery each time. The last time, however, Meckel's diverticulum was found, which probably accounted for the recurrence of the intussusception. It was not resected because of the poor condition of the boy at the time of operation, but the bowel was fixed to the abdominal wall at two points, in the hope that there might be no further recurrence.

BENJAMIN, Montreal, Canada.

A CONTRIBUTION TO THE STUDY OF THE LATE RESULTS OF SPLENECTOMIES FOR DISTURBANCES IN THE BLOOD. E. SCHNEEGANS, Rev. franç. de pédiat. **9**:256 (Feb.) 1933.

A boy of 12 years with the classic symptoms of thrombocytopenic purpura and The platelets increased to 450,000 after operation, and the child made an uneventful a platelet count of 86,000 was splenectomized in the author's clinic in Strassburg.

recovery. Four months later the boy reentered the clinic with a white cell count of 80,000 of which 98 per cent were lymphocytes. The condition progressed rapidly, and at death the lymphocytes numbered 505,000. Autopsy showed immense hyperplasia of the lymphoid tissue and unquestionable lymphatic leukemia. The author reviews the literature on reports of patients following splenectomy and concludes that great care should be taken in considering such a form of procedure until the true functions of the spleen are known and the relation that may exist between thrombocytopenia and leukemia is better studied. (In the light of Morquio and Volpe's article in the same issue of the *Revue française de pédiatrie*, these observations are of intense interest.)

SANFORD, Chicago.

VESICAL CALCULUS IN A CHILD AGED TEN YEARS: URINARY LITHIASIS IN CHILDHOOD. GENEROSO A. SCHIAVONE, Arch. argent. de pediat. **4**:41 (Jan.) 1933.

Urinary lithiasis in childhood is fairly frequent in South America, occurring usually between the ages of 2 and 8 years.

Lithiasis secondary to cystitis is rare.

The disorder can easily be confused with renal or vesical tuberculosis. Ureteral and vesical catheterization, rectal examination and, above all, roentgen examination usually establish the diagnosis, although the last mentioned diagnostic measure may at times give no information.

Treatment must be both medical and surgical. In many cases, there is spontaneous passage of the calculus. In renal and vesical calculus, operation is usually uncomplicated and successful. This is not always the case in ureteral calculus.

SCHLUTZ, Chicago.

VESICAL LITHIASIS IN A CHILD AGED SIX YEARS. SARA SATANOWSKY, Arch. argent. de pediat. **4**:60 (Jan.) 1933.

This condition occurred in a girl, aged 8 years. The calculus was of considerable size and was embedded in the posterior wall of the bladder. It was removed successfully by operation. The symptoms began at the age of 2½ years. The condition is rare in girls, particularly at that age.

SCHLUTZ, Chicago.

STRANGULATED INGUINAL HERNIA IN EARLY INFANCY. M. SERFATY and OSCAR R. MAROTTOLI, Arch. argent. de pediat. **4**:81 (Feb.) 1933.

The authors report four cases of strangulated inguinal hernia which occurred in infants aged 28 days, 3 months, 6 months and 14 months, respectively. They are of the opinion that there is some predisposition to this form of hernia in early infancy. Early symptoms of obstruction are not the rule in this age period, and this makes early diagnosis somewhat difficult.

Passing of blood by rectum may be observed early and is a valuable sign if a herniated mass is present. Early surgical intervention is by all means the best and most successful form of treatment.

SCHLUTZ, Chicago.

INDICATIONS FOR SPLENECTOMY IN VARIOUS HEMATOSPLENIC SYNDROMES IN CHILDHOOD. MAMERTO ACUNA, Arch. argent. de pediat. **4**:237 (April) 1933.

Splenectomy is the best treatment in the early phases of Banti's disease. It is of doubtful value in the later stages. It is seldom indicated in purpura haemorrhagica, except possibly in the very chronic forms described by Weil. It is almost without doubt the best form of treatment for congenital hemolytic icterus, most of the patients being completely cured. The optimal period for the operation is during the periods of remission of the icterus.

SCHLUTZ, Chicago.

MY EXPERIENCE IN THE TREATMENT OF POTT'S DISEASE. JOAQUIN DECREF, Med. de los niños **34**:46 (Feb.) 1933.

In an article running through four numbers of *Medicina de los niños*, the author describes the different methods of treating Pott's disease and their relative merits. In 1918, he presented 106 cases; there was a cure in 96, improvement in 9 and death from pulmonary tuberculosis in 1. The treatment consisted of supine decubitus. Decref has demonstrated by roentgenograms that when two or three vertebrae are fused to arrest the process, the adjacent vertebrae above and below acquire a greater capacity for extension so that the deformity is compensated.

The disappearance of the intervertebral disk does not necessarily mean tuberculosis. Vertebral arthritis, particularly in the cervical region, may be confused with tuberculosis.

The treatment advocated by the author is, briefly, as follows: 1. Pain should be relieved by immobilization and suspension. 2. The best position of rest is the supine decubitus in lordosis. 3. Rest is best obtained by the Lorenz or Redard bed. 4. Save for exceptional cases, laminectomy and transversotomy should be discarded. 5. The operations of Hibbs and Albee do not serve their purpose. 6. Heliotherapy has given the best results. 7. Sun baths are valuable indirectly because of their general effect on the organism. 8. Treatment with drugs consists in hydrominerals and serves as an adjunct to rest and heliotherapy.

Operation should be performed only in chronic cases in which the lesion has become localized. If the patient is operated on too early, the infection may be disseminated, and scar tissue is likely to be troublesome. Tuberculous abscesses are drained by aspiration as often as is necessary. The general treatment of rest in bed and heliotherapy has not been changed in fifteen years.

DWYER, Kansas City, Mo.

LATE RESULTS OF THE RAMSTEDT OPERATION FOR PYLORIC OBSTRUCTION IN INFANCY. G. CALINICH and R. ZENKER, Deutsche Ztschr. f. Chir. **239**:444 (March 2) 1933.

A clinical and roentgenographic study of nineteen patients observed from ten months to four years after a Ramstedt pyloroplasty showed a normal gastric emptying time in thirteen patients, a somewhat delayed emptying time with apparent weakness of gastric peristalsis in three and a slight narrowing in the region of the pylorus in three. In every patient development and nutrition were good.

GLASER, Rochester, N. Y.

APPENDICITIS IN CHILDREN AGED ONE AND ONE AND A HALF YEARS. E. FLUSSER, München. med. Wchnschr. **80**:609 (April 21) 1933.

Appendicitis in patients under 2 years of age is infrequent and difficult to diagnose. The diagnosis is usually not made until perforation has occurred. During fourteen years Flusser has seen eight patients under 1½ years of age with acute appendicitis, and in only one instance was the diagnosis made before perforation.

Abdominal pain is almost always present and is intermittent. Sometimes pain occurs shortly after food is taken. Tenesmus and urinary urgency without the passage of much urine are observed in some children. Tenderness over McBurney's point is difficult to elicit satisfactorily in most children, owing to lack of cooperation, but when it is present it is a valuable diagnostic sign. The author has found that the best time to examine a child is during sleep. If the child does not fall asleep, Flusser gives a suppository containing 0.2 Gm. of barbital (veronal). He has not found rectal examination as helpful as others have reported it to be. The presence of albumin, pus or blood in the urine does not necessarily exclude the presence of appendicitis.

BRAHDY, Mount Vernon, N. Y.

Miscellaneous

SPORTS TRAINING OF YOUTHS. ADOLPH JEZLER, Schweiz. med. Wchnschr. **63**:330 (April 8) 1933.

Thirty-four pupils of ages from 14 to 20 were clinically examined. Their vital capacity averaged 4.6 liters, and the systolic blood pressure, 127, although in some cases a value of 145 was observed. Tachycardia occurred only once during rest. The pulse rate averaged 71. After genuflexions the frequency was seldom abnormally increased, but in a majority of instances it did not return to normal within two minutes. The author advises medical oversight of training. Not more than four hours should be allowed weekly, and youths under 19 should be forbidden participation in violent contests.

VINTON, Brooklyn.

ANTHROPOMETRIC STUDIES OF THE JEWISH-ITALIAN CHILD. M. PAVIA, Riv. di clin. pediat. **31**:897 (Aug.) 1933.

Measurements were made of 190 Jewish children, aged 3, 4, 5 and 6 years, living in Padua; they were compared with the measurements of Italian children in the same city.

The Jewish child of 3 years is about the size of the Italian child of 5 years. In general, the Jewish child is bigger and develops faster physically than the Italian child.

HIGGINS, Boston.

SEROLOGIC INVESTIGATION OF TWINS. F. SCHIFF and O. V. VERSCHUER, Klin. Wchnschr. **10**:723 (April 18) 1931.

In this investigation, seventy-three monozygotic twins and eighty-eight dizygotic twins were studied. Among the latter were twenty-six pairs that differed in sex. In the monozygotic twins there was not an instance in which the partners of a pair did not belong to the same blood group. The findings in twins are in agreement with the known facts of the inheritance of blood groups and the inheritance of the serologic properties M and N. The regularity of the results in the monozygotic twins points to the factor N as a genetic quantity. This factor, like the factor M and the four blood groups, is distinct (*einwandfrei*). There is no evidence for different heredity in monozygotic twins. The serologic study of the blood groups and of the factors M and N may in some cases be an aid for the diagnosis of twins; discordance means arising from two ova.

SILVERMAN, Syracuse, N. Y.

THE SUCKING OF FINGERS DURING CHILDHOOD. M. SCHAECHTER, Med. Klin. **29**:1111 (Aug. 11) 1933.

Schaechter comments on the lack of knowledge of the significance of the sucking of fingers and on the disagreement among those who have written on the subject. Apparently, sex, age, nutrition and differences in feeding (from the breast or from the bottle) have little relation to the habit. The hypothesis that sucking of the fingers is caused by hypofunction of gastric secretion and represents a stimulus to such secretion is doubtful. If the lips are looked on as potential erogenous zones, long-continued sucking of the finger as a source of self-gratification may be harmful. Certain authors consider the habit to be a symptom peculiar to the neurotic child.

DOOLEY, Kent, Conn.

ULTRAVIOLET RAY-TRANSMITTING GLASS. K. WALTNER, Monatschr. f. Kinderh. **58**:195, 1933.

For three years the author studied the properties of one of the best advertised German therapeutic window glasses. He found it worthless as regards the transmission of ultraviolet rays. He does not mention the name of the manufacturer.

GERSTLEY, Chicago.

POISONING WITH ETHYL AMINOBENZOATE IN INFANCY. B. EPSTEIN and F. HENDRYCH, Monatschr. f. Kinderh. **58**:358, 1933.

A child of a tuberculous mother suffered from severe purulent pharyngitis and repeated vomiting. The stomach was washed with a 5 per cent solution of ethyl aminobenzoate (anesthesin) and at the same time some of the dry powder was blown into the pharynx. One cubic centimeter of horse serum was given subcutaneously for protein therapy. Shortly afterward, the child went into collapse with severe cyanosis from a resulting methemoglobinemia. Recovery followed stimulation. The writers attribute the symptoms to the ethyl aminobenzoate rather than to anaphylactic shock.

GERSTLEY, Chicago.

TEETH OF ZURICH CHILDREN FROM FOUR TO SIX YEARS OF AGE. BERTA NIGGLI-HURLIMANN, Verhandl. d. schweiz. naturforsch. Gesellsch. **113**:390, 1932.

This article reports an additional study of kindergarten children. As a rule, children 4½ years of age have a complete set of milk teeth. In girls the teeth develop somewhat earlier than in boys. At the age of 4½ years 2.2 per cent of the girls already had their lower incisors; only 1.6 per cent of the boys had a single first incisor at 5 years. In the upper jaw eruption of the permanent teeth begins about half a year later, in the same order as in the lower jaw. Here again girls are about half a year ahead of boys. The milk teeth decay markedly between the ages of 4½ and 6½ years. In the lower jaw there is a greater contrast between individual teeth. The author did not observe a difference between poor children and those of a better class. Only about one child in five required treatment at this age. Inasmuch as the molars of the milk teeth must serve up to 9 or even 11 years of age, closer attention should be given to them.

VINTON, Brooklyn.

LEFT-HANDEDNESS, WITH OBSERVATIONS ON STUTTGART SCHOOL CHILDREN. M. SCHILLER, Ztschr. f. d. ges. Neurol. u. Psychiat. **140**:496 (July) 1932.

Schiller gives a brief historical review of left-handedness and quotes statistics to show that the incidence of left-handedness increases as one passes from east to west (from 4 per cent in Russia to 13 per cent in Alsace), that the incidence is greater in males than in females, and that its transmission is probably hereditary. In the literature, left-handedness is linked with feeblemindedness, epilepsy, crime and disturbances in speech. Varying grades of left-handedness are observed, from the dominant to the ambidextrous and the latent type. The ability to produce mirror writing is a classic symptom of left-handedness.

The author's own figures, compiled from a study of about 1,800 children in the Stuttgart schools, show the incidence of left-handedness to be 7 per cent, 10 per cent of which was in boys and 6.6 per cent in girls. A family history of left-handedness was obtained in 54 per cent of cases and, on careful inquiry, in as many as 80 per cent. In the special schools for retarded children no greater incidence of left-handedness was found. Half of those who were left-handed were also left-eyed as determined by a method of sight-testing. Left-eyedness occurred twice as frequently in cases in which a family history of left-handedness was obtained.

Schiller found a causal relationship between disturbances in speech and left-handedness: Seventeen per cent of the stutterers were left-handed. If cases of left-eyedness, left-footedness or mirror writing with the right hand were included, this figure rose to 36 per cent. Among younger school children there seemed to be a relationship between left-handedness and dyslalia, as well as between left-handedness and stuttering. In 50 per cent of the latter cases the children were left-handed. Mirror writing was pathognomonic of left-handedness or left-eyedness. The author believes that left-handed children should not be trained to use the right hand.

WOLF, Paterson, N. J.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

Scientific Sessions, Asheville, N. C., May 3-5, 1934

CHARLES A. FIFE, M.D., *President, in the Chair*

(*Concluded from page 701*)

Fourth Session

Friday Evening, May 4

PRESENT STATUS OF THE PROBLEM OF RHEUMATIC FEVER. DR. T. DUCKETT JONES (by invitation), Boston.

A short discussion of the clinical picture of chronic, low grade rheumatic fever and heart disease, with especial emphasis on the course of the disease, as shown by a group of 1,000 cases, is given. The rôle of chorea as a rheumatic infection is elaborated on, since analysis of the records does not bear out the belief which seems established in every one's mind that chorea is a grave manifestation of rheumatic fever.

The etiology of rheumatic fever is discussed. A review of the literature as to conceptions of the possible or probable rôle of streptococci as a cause of rheumatic fever brings out the following theories: (1) the theory that a specific streptococcus causes the disease by elaborating a specific toxin, (2) the elective localization theory of Rosenow and (3) the allergic hypothesis.

The relationship between respiratory infection and recurrences of rheumatic fever is discussed, and an analysis of work based on throat cultures from patients with rheumatic fever and controls is outlined. A general summary of the climatic and geographic distribution of rheumatic fever and its implications is given, and the transportation of patients with rheumatic fever to the warmer climates of Peurto Rico and Miami Beach as a method of treatment is reported on. This is followed by a discussion of the measurement of immune bodies in rheumatic fever.

The production of manifestations of rheumatic fever or recurrences in human beings with the use of nonspecific protein shock (typhoid vaccine) has been successfully accomplished.

DISCUSSION

DR. HUGH MCCULLOCH, St. Louis: I should like to express my appreciation to Dr. Jones for describing his work on this subject. I agree so well on the fundamentals that it is rather difficult to find a point on which to differ. One has to get out of the zone of realities and facts to bring up matter for discussion.

Dr. Jones traced well the many difficulties confronting physicians in working out the relationship of respiratory infections to the recurrences of rheumatic fever. There are one or two points on which perhaps one may disagree and which one might discuss. One is the extreme difficulty of determining clinically when a child suffers from a respiratory infection. When one sees definite signs it is a simple problem. But in rheumatic subjects the degree of infection which may incite a subsequent attack of rheumatic fever may be so slight as to be difficult to recognize. It is somewhat easier to recognize the preceding infection if the children are under constant observation and the temperature is being recorded and daily inspections of the nose and throat are being made, but in clinics, especially in outpatient departments, recognition may be difficult.

I should also like to point out the fact, with which Dr. Jones is well acquainted, that all bacteriologic methods used at present for the study of the flora of the respiratory tract are crude. Further refinements may show a closer relationship

of these infections to attacks of rheumatic fever. Dr. Dochez' report last year showed that the bacterial flora may be difficult to classify without refined methods.

Dr. Jones interpolated some remarks about chorea which interest me. Chorea and rheumatic heart disease are collateral offspring of the parent rheumatic state, and it is not fair or accurate to try to trace the one to the other; that is, chorea to rheumatic heart disease.

I have been impressed recently with the fact that a great many patients with chorea may not show other manifestations of rheumatic fever at any time. In searching about for an explanation of this I have been struck by two things. One is that many of the patients who are classified as having Sydenham's chorea may not have that. They may be hyperkinetic or hypermotive, and under strain may break down with movements that resemble chorea closely. A great many of these patients show little evidence of respiratory or other infection.

The second consideration is illustrated by the group of somewhat older children who tend to be obese and who show some of the symptoms of mild hypothyroidism. It is possible that the ones who show motor along with emotional instability during this period have not true rheumatic chorea. It is possible that some of the patients who are considered to have chorea and do not subsequently show heart disease have not had rheumatic chorea to begin with.

Dr. Charles Hendee Smith, New York: I wish to say a word lest some one may interpret Dr. Jones' results following a single injection of typhoid vaccine in subacute rheumatic fever as an argument against the fever treatment for chorea. I occasionally see rheumatic fever in a patient with chorea, but in the patients with chorea treated by fever therapy I have not seen any stirring up of the rheumatic process. A single dose producing a relatively low fever may act quite differently from doses producing a high fever every day or every other day or over a single long period (as in the hot box treatment).

There are three difficulties in this problem: 1. It is not always easy to decide whether a given patient has a respiratory infection. 2. It seems to be difficult for many physicians to tell whether a patient has chorea. A surprising number of patients are referred to our chorea class who have not Sydenham's chorea. Of course, no one ought to mistake an ordinary habit spasm for chorea. But post-encephalitic chorea is not uncommon. In addition, I have seen a number of children who have symptoms of classic chorea, but who have had it practically all their lives. This may possibly represent some vascular damage in the basal ganglions at birth. 3. The final difficulty that complicates the whole study of rheumatism is in telling when the patient has active rheumatic fever. As an example, I recently observed a child with mild acute rheumatic fever and delayed conduction time, showing some involvement of the heart. After a time all the symptoms disappeared. He had no fever. The blood showed a normal rate of sedimentation; the white count was normal, and there was no increase in immature forms. There were a mitral murmur of a mild degree and questionable enlargement of the heart. The child became excited while playing ball with his father; edema of the lungs developed, and he died within a few hours. His heart showed a great many Aschoff bodies, more than are often seen. There was no clinical method of recognizing the fact that the child still had active carditis. A better means of determining activity in this disease is needed.

Dr. Samuel Z. Levine, New York: I should like to mention briefly the work that Dr. Wilson has done within the past year in the cardiac clinic of New York Hospital, especially emphasizing some of the points brought out by Dr. Jones.

She has carried on intensive studies on a group of rheumatic and nonrheumatic children to obtain information as to the possible relationship of respiratory infections to the recrudescences of rheumatic fever. These studies included observations of the seasonal flora of the throat and the antistreptolysin content of the serum, as well as close observation of the clinical course of rheumatic fever. From these studies she obtained evidence which does not support the conception of a specific etiologic relationship between respiratory infections and rheumatic fever.

DR. SAMUEL W. CLAUSEN, Rochester, N. Y.: In studying the possible occurrence of subclinical scurvy in children with rheumatic fever, Dr. J. D. Keith and Dr. Mary Clayton of Rochester determined the ascorbic acid content of the blood, urine and tonsils. They found no differences between nonrheumatic and rheumatic children. It therefore seems likely that subclinical scurvy plays no rôle in rheumatic fever.

DR. T. DUCKETT JONES, Boston: I should like to thank both Dr. McCulloch and Dr. Smith for what they said about chorea. All the patients with chorea were seen over a period of months and were continuously observed by five or six different physicians who are thoroughly competent. All agreed on the diagnosis. There were many cases which were not included in this study for various reasons and were not accepted as being instances of Sydenham's chorea.

I am especially glad that Dr. Smith called attention to the work of Dr. Sutton in using typhoid vaccine in the treatment of chorea. The work referred to in my paper is in no sense similar to that of Dr. Sutton with therapeutic inoculation of vaccine and in itself is neither an indication nor a contraindication for the therapeutic use of typhoid vaccine. I appreciate also the remarks of Dr. Levine concerning Dr. Wilson's work and am glad that we are in accord.

A BACTERIOLOGIC STUDY OF PNEUMONIA OVER A SIX YEAR PERIOD. DR. JAMES OWLING TRASK, New Haven, Conn.

An attempt was made to establish a bacteriologic diagnosis for the 600 patients with pneumonia, empyema and bronchitis admitted to the peditaric wards from July 1927 to June 1933. Success was attained in about 75 per cent. The following general groups could be distinguished: (1) pneumococcic pneumonia, (2) mixed pneumococcic and influenza bacillus pneumonia, (3) influenza bacillus pneumonia, (4) hemolytic streptococcic pneumonia and (5) staphylococcic pneumonia. Mixed infections were the outstanding feature of group 3, but they were common in the other groups as well and made classification difficult. However, the five groups of pneumonia were analyzed in respect to age and seasonal incidence, predisposing cause, bacteremia, clinical diagnosis and outcome. The results showed that type 1 pneumococcic pneumonia was the prototype of lobar pneumonia in children 2 years of age and over. Mixed pneumococcic and influenza bacillus pneumonia corresponded to the usual bronchopneumonia of infancy and early childhood. Influenza bacillus pneumonia corresponded to capillary bronchitis. Hemolytic streptococcic pneumonia was represented by a severe highly fatal pneumonia in which early empyema developed. Staphylococcic pneumonia was characterized by abscess formation and high mortality.

DISCUSSION

DR. BÉLA SCHICK, New York: At Mount Sinai Hospital Dr. Louis Rauh and Dr. Newman have made an investigation along this line for more than two years. Of 109 cases studied pneumococci were found in about 70 per cent. In the younger age group type 14 is the predominant organism. Types 7, 8 and 29 are next in frequency. All other types are relatively rare. Serum treatment is not used. Dr. Bullova is enthusiastic about the serum treatment of the different types. It was interesting to see how mortality at Mount Sinai Hospital compared with that at other hospitals. Of course, it is difficult to compare cases of pneumonia of different hospitals, because some hospitals get more severe cases than others. The mortality from pneumonia in my department was relatively low (15 per cent). Therefore, I do not think that the results would have been improved by serum treatment.

DR. CHARLES HENDEE SMITH, New York: We have been fortunate to be practically at the headquarters of this Cooper differentiation of types, under Dr. Park in the New York City Health Department. Since 1928 we have been able to have these types differentiated as fast as they were discovered.

I believe that it is important to separate the different types of the old group 4, because the prognosis is different, and their response to serum is different. Many

of the members may have read Dr. Nemir's recent article in the *Journal of Pediatrics* on the first few years of the serum treatment at Bellevue Hospital. Pneumococcus type I responds well to serum in children, as it does in adults. Type 14 responds almost as well, and a few others seem to respond partially, though not as well as types 1 and 14.

The difficulty is that types 1 and 14 are usually found in older children, in whom there is relatively low mortality. In infancy, when the mortality is high, unfortunately there are more cases of the types for which there is no serum. There are about 17 serums available at present.

The shortening of the disease is the main test of the efficacy of the serum. We believe that it has been shown definitely that the course of pneumococcic pneumonia can be shortened if the patient is treated early.

Of course, the mortality from uncomplicated pneumonia in older children is not high, but if any child dies it is 100 per cent for him. In some of our controls of group types 1 and 14 and in some other patients from whom we withheld the serum complications developed, and the patients died, making us regret not having used it.

It seems to me that this treatment will probably be used more in the future, in spite of the difficulty and expense of typing and producing the serums.

DR. JAMES DOWLING TRASK, New Haven, Conn.: The results reported show that serum treatment accomplishes something—mainly a shortening of the duration of the disease. It is not clear of how much practical value this is going to be, because the serious pneumonias in childhood are due to infections with the influenza bacillus, the hemolytic streptococcus and staphylococci.

OCCURRENCE OF STREPTOCCOCUS HAEMOLYTICUS IN THE THROATS OF CHILDREN IN HOSPITAL WARDS. DR. LEO B. BURGIN (by invitation) and DR. HAROLD L. HIGGINS, Boston.

The incidence of Streptococcus haemolyticus in throats was as high in a ward for patients with noninfectious conditions of the eye as in a ward in which there were many patients with suppurative infections of the ear and nasal sinuses. Thus, the incidence of carriers seems to depend more on prevalent epidemic respiratory infections than on the presence of patients with more or less chronic infections. The members of the nursing staff of a children's hospital are certain to become carriers of Streptococcus haemolyticus at one time or another. The percentage of carriers among tonsillectomized children is less than among those still having their tonsils.

DISCUSSION

HENRY DIETRICH, Los Angeles: The Certified Milk Commission of Los Angeles has been interested in the question of streptococcic contamination of milk. They have limited their study to Streptococcus epidemicus of the scarlet fever type, if one may speak of two types. They have not studied Streptococcus pyogenes.

The commission has investigated the personnel in dairies supplying certified milk. Among that personnel, over a period of two years, were found 48 carriers. Some of these were kept under observation for a year. In no case was it found that the condition cleared up spontaneously in one who had hypertrophied tonsils.

Thirty-two of the 48 carriers submitted to operative removal of the tonsils. In all but 7 a negative culture was promptly obtained. In the 7 in whom the cultures still remained positive, subsequent removal of small pieces of tonsillar tissue or lymphoid tissue in the lingual tonsil promptly resulted in negative cultures.

In all the 32 patients who submitted to this operative procedure the condition was cleared up. Many of the men have been examined monthly since that time over a period of years and have given negative cultures.

The details of this work will be reported at the meeting of the American Public Health Association by the director of the laboratory.

ENCEPHALITIS. DR. THOMAS MILTON RIVERS, New York.

Encephalitis is an inflammation of the brain and can be induced in a number of ways. This presentation is limited to inflammations of the central nervous system caused by viruses. A list of the natural and experimental virus-encephalitides of man and lower animals is given. Comment is offered concerning: (1) the manner in which viruses enter and spread through the central nervous system and (2) the pathologic pictures produced by their activities in the brain and spinal cord. Finally, epidemic encephalitis, the encephalitis that occurred in St. Louis in 1933, Japanese summer encephalitis (type B encephalitis), Australian X disease and postinfection encephalitis (postvaccinal and postmeasles encephalitis) are compared with regard to epidemiology, clinical findings, pathologic pictures, etiology and immunologic phenomena.

Fifth Session

Saturday Morning, May 5

INTRAVENOUS ADMINISTRATION OF FAT FOR THERAPEUTIC AND DIAGNOSTIC PURPOSES. DR. L. EMMETT HOLT JR., DR. HERBERT C. TIDWELL (by invitation) and DR. T. F. MCNAIR SCOTT (by invitation), Baltimore.

A technic for preparing emulsions of fat that can be given intravenously with safety was developed by Japanese investigators ten or fifteen years ago. By means of lecithin the emulsions are rendered sufficiently stable to resist sterilization by heat. When the emulsified particles do not exceed 2 microns in diameter, the danger of fat embolism is abolished. There is some experimental evidence that fat so introduced is utilized in a normal manner.

Our own observations consist in: (1) comparisons of the rate of disappearance of fat from the blood when different fats are introduced intravenously in infants, (2) clinical observations on the use of intravenous fat in nutritional disorders and (3) certain observations on the lipemic curve after fat is given intravenously in pathologic conditions.

We have not been able to discover differences between particular fats by means of the rate of disappearance. The rate of removal from the blood appears to be determined by the emulsifying agent.

Certain clinical observations suggest that fat given intravenously is of value as parenteral food in nutritional disorders.

After the intravenous administration of fat the lipemic curve appears to give some information as to whether this material can be readily used. A small rise and prompt fall we have interpreted as an indication of ease of utilization, and a large rise and delayed fall as an indication of the reverse.

DISCUSSION

DR. SAMUEL Z. LEVINE, New York: Dr. Holt was kind enough to supply us with a quantity of this material, and we have had a fair opportunity to use it in a number of cases, for experimental rather than for clinical purposes.

I can confirm the statement made by Dr. Holt that the procedure is almost absolutely safe. There was never any reaction, though forty or fifty injections were given to different types of children.

Most of the material was utilized in attempting to determine the combustion of this fat in the human body. Obviously, if the fat is to be of any value in the body of the infant, it must be utilized for purposes of energy. When the fat is given it is taken up by the blood, as Dr. Holt pointed out; then it is either burned directly or lost in the urine or in the stools. If it is burned directly, it should have a direct effect on the respiratory quotient and possibly should affect the protein metabolism.

We have been brave enough to give not 1 Gm. per kilogram of body weight to some of the infants, but as much as 5 Gm. per kilogram! Analysis of the

stools for ether-soluble residue has not thus far shown any increase following injection. Therefore, in those instances the fat must have remained in the body. However, we were not able to demonstrate conclusively that it was burned, at least shortly after its injection.

In 1 infant the respiratory quotient in a number of observations dropped appreciably—to point 5 in the second place, which is the level of the fall when fat is injected into normal infants. However, in this infant there was no reduction of the nitrogen (protein metabolism) for forty-eight hours following the injections of fat.

When Dr. Holt said that the evidence thus far was suggestive, he was well within his rights. However, as he pointed out, the evidence is not conclusive.

DR. F. B. TALBOT, Boston: When fat is given in large amounts in the ketogenic diet, in which nearly 90 per cent of the calories may be in the form of fat, one expects a marked increase in the urinary protein, if more protein is burned to give the antiketogenic element necessary to oxidize the fat.

For the past year, my associates and I have been making a study of the blood sugars and the respiratory quotient, as affected by diet. With a diet high in fat there may be a pure fat respiratory quotient of 0.7 or even less, and yet no significent rise in the urinary protein—a rather surprising result. There is also marked lowering of the circulating blood sugar; in some cases it was well below 80 mg. per hundred cubic centimeters. When meals high in fat and low in carbohydrate were given there was not the expected rise in either the respiratory quotient or the blood sugar after the meal.

DR. LOUIS C. SCHROEDER, New York: It is gratifying to learn that there is a renewed interest in the possibilities of utilizing fat intravenously. It is also of interest that Dr. Holt believes that there is some correspondence between the amounts of fat determined by chemical methods and those determined by Gage's method of counting chylomicrons.

I should like to ask Dr. Holt whether he has made any subcutaneous injections with this particular form of fat. At one time, especially in sanatoriums for tuberculosis, a great deal of work of this nature was done, but the inherent risks never led to the use of this therapy to any wide extent. Experiments on animals indicated that the dangers of cutaneous necrosis were great. Apparently there is much hope that better results may be obtained with the newest forms of fat.

It is also likely that a further happy result of this study will be a better understanding of the physiology of fat. When working some years ago with butter stained with sudan III, I found it possible to give nursing mothers this form of fat and produce distinctly pink breast milk. Gage had produced the same results in lactating animals and asked a number of exceedingly interesting questions as to the fate of the fatty acid radicals first injected, which remain unanswered to this day. It is not unlikely that such work as Dr. Holt has started will provide the answer to many questions of interest about fat and its utilization.

DR. BÉLA SCHICK, New York: Several years ago I was interested in this question. I injected oil subcutaneously, and it was absorbed slowly. The procedure was used for several days in the treatment of a child whom it was almost impossible to feed after an operation for Hirschsprung's disease.

As Dr. Schroeder mentioned, the literature shows satisfactory results in patients with tuberculosis.

I consulted Dr. Lusk. In his laboratory one study was made with the injection of oil. The first injections of oil were absorbed well; further injections were absorbed more slowly. One child showed, after a while, what is known as a foreign body reaction, which is very unpleasant.

My impression is that intravenous injection is preferable. The further increase in weight may be checked. I should like to know whether Dr. Holt made observations as to the retention of water. Retention of water may explain partly the maintenance of weight.

DR. DANIEL C. DARROW, New Haven, Conn.: What methods are used for determining the fats?

DR. L. EMMETT HOLT JR., Baltimore: In reply to Dr. Schroeder's question, we have not made any studies with subcutaneous injection of fat. Dr. Schick really answered the question. He made such studies.

It would be very interesting to study the retention of water. We have not done that to date, but it is a good suggestion.

In regard to Dr. Darrow's question, the method we used was a modification of the procedure devised by Dr. Görter, which was described before the society last year. The determination was made on an ether extract of dried whole blood. This fraction contains all the neutral fat and free cholesterol and a part of the cholesterol esters, but no phospholipids.

We made a rather interesting observation with fat stained with sudan III injected into an adult with nontropical sprue. The stools of this patient gave no indication of the presence of the dye, but when we added hydrogen chloride and heated the mixture the red color of sudan III developed promptly, showing that a considerable amount of dye and probably of fat as well had entered the intestine from the blood stream. This supports the view of Dr. Bauer that there is a secretion of fat into the bowel in celiac disease.

PREVALENCE OF VITAMIN A DEFICIENCY AMONG CHILDREN IN IOWA. DR. P. C. JEANS and ZELMA ZENTMIRE, M.S., Iowa City.

A test has been devised which is believed to detect moderate degrees of vitamin A deficiency. The procedure consists in measuring the sensitivity of scotopic vision to light under standardized conditions. Subnormal sensitivity to light is related to functional night blindness, a result of vitamin A deficiency.

Among the school children of an Iowa county a survey with this test showed 26 per cent of the rural children and 53 per cent of the town children to be deficient in vitamin A. A similar survey in Des Moines showed a still higher percentage of vitamin A-deficient children. The study is still being actively pursued, and the vitamin A-deficient group is being retested after receiving vitamin A from a special source. It is indicated that a routine hospital diet without additional vitamin A supplies sufficient vitamin to produce normal readings with the test in all but exceptional children.

DR. A. A. WEECH, New York: It is gratifying to have listened to Dr. Jeans' description of a tangible method for measuring a subclinical deficiency disease. It is to be hoped that diagnosis in the future will depend on this method and similar methods rather than on vague symptoms, such as general malaise, susceptibility to infection and anorexia, which are common to a thousand and one different disorders. Recently, an attempt has been made to utilize the capillary resistance test as a means of recognizing latent vitamin C deficiency in a given population.

During my sojourn in China I came in contact with the more serious aspects of vitamin A deficiency, that is, with keratomalacia. The disease is fairly frequent in both children and adults. Dr. Pillat, who studied the occurrence in adults, found a seasonal incidence, which corresponds to the period when the intake of green vegetables is at low ebb, namely, late winter and early spring. We were surprised to find two peaks in the annual incidence curve in children. One peak was the same as that which Dr. Pillat had found in adults, and the other occurred in August in association with protracted and severe dysentery. It seemed that prolonged diarrhea interfered in some way with the absorption of vitamin A and so favored the outbreak of acute symptoms of deficiency disease.

The apparent widespread incidence of vitamin A deficiency is astonishing, and I find it difficult to understand why accessory factors do not operate occasionally to produce the more outstanding manifestations. The absence of occasional cases of keratomalacia leaves me a little skeptical about the interpretation which has been placed on the results, but it would be interesting and instructive to learn whether the test reveals a seasonal incidence of latent vitamin A deficiency and also whether prolonged diarrhea is associated with lowered ability to adapt vision to the dark.

DR. P. C. JEANS: We have made observations with the vitamin A test other than those discussed, but they cannot be included under the title submitted for this presentation. Some of the observations were in relation to diarrhea and the use of mineral oils. Undoubtedly, both of these have an effect on the utilization of vitamin A, though I have no data at hand which I can present in support of this statement. We do not yet have evidence concerning seasonal variations in vitamin A deficiency.

A COMPARATIVE STUDY OF BLOOD IRON AND HEMOGLOBIN IN PREMATURE INFANTS. DR. ARTHUR F. ABT (by invitation), Chicago.

In studying the anemia of premature infants the problem of the relationship of the iron content of the whole blood to the hemoglobin content was considered worthy of investigation. This report is based on simultaneous determinations of the iron and hemoglobin in the whole blood of a group of normal healthy premature infants from birth to 8 months of age.

From the determinations it is evident that the highest values of whole blood iron occurred in the neonatal period. There was a weekly decrease, the lowest point being reached about the twelfth week of age. Thereafter the curve remained level, with a slight peak at the fifth month. The hemoglobin curve closely followed that of the whole blood iron. Comparison of the curve of the actually determined iron with that of the iron calculated from the determined hemoglobin by the Butterfield factor showed an approximation within the limits of experimental error.

The hemoglobin-whole blood iron ratio determined for this group of premature infants agreed closely with the same ratio as determined by Katikoff for a group of full-term infants.

Whole blood iron was determined by the Foweather method. Control duplicate determinations on older infants and adults showed that this method was consistently reliable. Williams' improved Newcomer hemoglobinometer was used for the determinations of hemoglobin.

The various factors concerned in the production of the physiologic anemia of premature infants were discussed in relation to the determinations reported for blood iron and hemoglobin.

DISCUSSION

DR. HUGE W. JOSEPHS, Baltimore: I can confirm Dr. Abt's figures for the relation between the hemoglobin values as determined by the Newcomer method and as calculated from the total iron in premature babies. The expected relationship holds in normal blood and even in anemic blood. This has led to the suggestion that the total iron of the whole blood be used as a means of determining the hemoglobin. There are certain conditions, however, in which the expected relationship does not hold, the total iron exceeding the hemoglobin iron by a measurable amount. For example, in full-term babies the total iron exceeds the hemoglobin iron during the first two months of life by 25 per cent or more. This means that there is considerable iron in the blood above what can be accounted for by the hemoglobin, when this is determined as acid hematin. The significance of this extra iron is unknown.

DR. ARTHUR F. ABT, Chicago: I had the opportunity, while conducting this study on the hemoglobin and whole blood iron of premature infants, to observe a new-born premature infant suffering from icterus gravis with erythroblastosis. There was a marked difference in the value of whole blood iron determined from the value for iron calculated from the determined hemoglobin. I attribute this discrepancy to the extreme hemolysis which occurs in icterus gravis neonatorum.

SIZE AND HEMOGLOBIN CONTENT OF RED BLOOD CELLS IN INFANTS AND CHILDREN IN NORMAL AND ANEMIC STATES. DR. GEORGE MARTIN GUEST, Cincinnati.

Values for the size of the red blood cells, and for their hemoglobin content (listed by various authors as corpuscular hemoglobin, hemoglobin saturation index,

etc.) have been used extensively in the classification of anemias in adults, but such data for infants and children are comparatively few. In the studies reported here the following data have been collected and analyzed: (1) the cell volume in per cent of whole blood, determined by an improved capillary tube method described by Guest and Siler in 1934; (2) the red cell count in millions per cubic millimeter of blood; (3) the size of the erythrocyte in cubic microns, obtained by dividing the figure for cell volume by the cell count; (4) the hemoglobin content listed in three ways, namely (*a*) the hemoglobin in whole blood, in grams per hundred cubic centimeters, (*b*) the hemoglobin in cells, in grams per hundred cubic centimeters of packed cells and (*c*) the hemoglobin-red blood cell count quotient which is the figure for grams of hemoglobin per hundred cubic centimeters of whole blood divided by the cell count, an expression of the amount of hemoglobin contained in the average individual cell. Attention is directed particularly to the values for

Size and Hemoglobin Content of Red Blood Cells in Representative Subjects in Normal and Anemic States

Subjects	Red Cells, Volume per Cent	Red Cell Count, Millions per C.Mm.	Size of Erythrocytes, Cubic Microns	Hemoglobin		
				Whole Blood, Gm. per 100 Cc.	Cells, Gm. per 100 Cc.	Hemoglobin : Red Blood Cell Count Ratio
Boy, 8 years old, "normal"....	38.1	4.468	85.3	13.59	35.7	3.04
Mother of the new-born infant	38.0	4.223	90.0	13.12	34.5	3.11
New-born infant.....	69.1	5.933	116.5	21.96	31.8	3.70
1 month.....	51.0	5.028	101.4	16.42	32.0	3.27
4 months.....	35.3	4.376	80.7	11.10	32.4	2.54
6 months.....	37.3	5.505	67.8	11.44	30.7	2.08
8 months.....	37.9	5.491	69.0	11.50	30.3	2.09
Boy, 2½ years old, with nutritional anemia.....	15.2	2.980	51.0	3.42	22.5	1.15
Treated with iron and copper						
2 weeks.....	28.5	4.030	70.7	7.45	26.1	1.85
1 month.....	36.0	4.610	78.1	10.24	28.4	2.23
4 months.....	39.7	4.820	82.4	13.92	35.1	2.89
Boy, 14 mos. old, with anemia of lead poisoning.....	22.5	3.770	59.7	6.89	30.6	1.83
Treated with iron and copper						
6 weeks.....	35.5	4.720	75.2	11.71	33.0	2.48
4 months.....	34.8	4.140	84.1	12.27	35.3	2.96

size of the erythrocyte and hemoglobin in cells, as these have proved especially helpful clinically.

In the blood of normal infants followed from birth a striking change observed during the first six months or longer is a progressive decrease in size of the erythrocyte, from a size considerably larger to one considerably smaller than the average found in older children. In nutritional anemia—the microcytic hypochromic type that responds well to dietary treatment and the administration of iron and copper—these studies afford a good measure of control on the effects of treatment. The table lists representative values selected from a series for approximately 400 samples of blood from more than 50 adults, 150 children and 25 new-born infants.

DISCUSSION

DR. ALFRED H. WASHBURN, Denver: Knowing something of the difficulties of doing accurate work on the red cells and hemoglobin, I wish to congratulate Dr. Guest on what I think is a beautiful piece of work, accurately done and nicely presented. I am much interested, as my associates and I are attacking much the same problem.

There are some questions which I should like to ask Dr. Guest and some comments which I should like to make. I should like to know his reaction as to whether one can assume that studies on intravenous blood removed by venipuncture are comparable to those on peripheral blood obtained by a prick. I have my doubts, and there is some evidence that these doubts are justified. I should like to have him state whether he has had any experience with the comparison of blood obtained in the usual clinical manner and that obtained by venipuncture.

As to the comparison between cord blood and peripheral blood obtained in the new-born, we have been getting poor agreement, and I should like to know whether he has had any experience in that.

I am particularly interested and wish to reemphasize Dr. Guest's insistence on recording hemoglobin either in grams or in terms of percentage, noting what the method is and what the percentage means in terms of grams. I agree with him that there has been a great deal of confusion, and when one goes to the literature it is difficult to make comparisons between reports and one's own work.

I should also like to comment on the last point which he mentioned: that nutritional anemia represents an exaggeration of a more or less physiologic cycle. In practically every normal new-born baby whom I have studied, when there has been no iron or copper therapy nor any solid addition to the formula, there have been curves similar to the ones shown by Dr. Abt and Dr. Guest. Starting at a high point, coming down and dipping below the normal, the curves then show a turning point at the age of 2 or 3 months, coming back and sometimes rising above the normal and then settling down to that level.

If that is the case, one should be extremely cautious in interpreting the results of such therapy as treatment with iron and copper at this time, when there is apparently a tendency in the average infant to return to the normal level. When this picture occurs at 9 months of age, one has a different situation. When the descent is at 2 or 3 months of age, one must be careful not to draw conclusions from therapy, unless it is carefully controlled by a normal series.

DR. T. B. COOLEY, Detroit: I have been interested during the last year or so in studying fragmentation, which is the ordinary process for disposing of the red blood cells as related to some of the anemic states. I have become satisfied that it is a common factor in a great many of the anemias of childhood.

One part of the fragmentation is fission of the cell, with the production of two microcytes. Another is the breaking off of small portions, leaving larger fragments behind. If blood in which such a process is proceeding is studied by hematocrit determinations, a relatively low volume index is obtained, which might be deceptive if one were going to use the methods which Hayden and Wintrobe are urging for classification of the anemias. It would disturb some of the indexes considerably. If one is to make good use of these indexes, one must, in a number of cases, determine from study of the stained smear or, better, of the fresh moist film whether much fragmentation is going on.

It has long been customary to state in descriptions of blood films the amount of anisocytosis and poikilocytosis. I am satisfied that if these are marked it means that there is a great deal of fragmentation, in which case some of the indexes of which Dr. Guest spoke would have little significance, unless controlled by measurements by the Price-Jones method.

Why fragmentation should be so marked in some of these anemias I am not sure. I think that sometimes it may be merely because few young cells are coming into the circulation, which makes the disintegration of the old ones more prominent. When the size of the cells in the stained smear is comparatively uniform, the situation is different. This would indicate little fragmentation, and the various indexes would be more dependable.

DR. ALFRED T. SHOHL, New Haven, Conn.: I should like to ask Dr. Guest whether these figures which one has always considered to be normal represent an unavoidable condition of the blood or whether they represent the present status with regard to the nutritional intake not only of iron but also of vitamins in relation to blood formation.

DR. GEORGE MARTIN GUEST, Cincinnati: To answer Dr. Washburn's question, in some circumstances considerable differences may be found between the cell counts and the hemoglobin values of blood samples obtained in different ways —from the cord or from other peripheral vessels—from one infant. Such differences are due, for the most part, to local conditions of the tissues, such as stasis, which can lead to changes in the proportions of cells and plasma in the whole blood. In such samples of blood, however, the calculated values for the size and hemoglobin of the erythrocytes should not differ significantly. Physiologists have demonstrated slight changes in the size of erythrocytes with respiratory exchange, but those changes are so small as to be insignificant in these clinical studies.

The progressive fission of red cells, which Dr. Cooley describes as taking place in certain bloods, is an interesting phenomenon, but such changes do not necessarily need to be considered in making practical use of the measurements described here. The values which have been discussed serve as an expression of certain characteristics of the average cells in a given sample of blood at the time of examination, and it is not implied that these characteristics are static.

I do not believe that any data now available justify a definite answer to Dr. Shohl's question as to what degree of variability in these values may be considered normal. The determination of average values for any group of infants is easier than the recognition of what should be considered as normal or, even more difficult, what should be considered an optimum level for these values. With regard to hemoglobin, this question has been discussed in recent papers by Elvehjem in this country and by Mackay in England. Newer knowledge of the influence of diet and varying mineral balance on these values is likely to change current views concerning the level at which hemoglobin may be maintained in children under optimum dietary conditions.

INFLUENCE OF PLASMA AND PLASMA EXTRACTS ON THE COURSE OF HEMOLYTIC ANEMIA. DR. HUGH W. JOSEPHS, Baltimore.

The treatment of the type of congenital hemolytic anemia represented by both congenital hemolytic jaundice and sickle cell anemia presents two related problems: (1) the raising of the general level of the hemoglobin and (2) the prevention or abortion of the hemolytic crises.

The starting point of the work reported here was the observation that transfusion in a case of sickle cell anemia caused immediate reduction in the daily excretion of urobilin in the stools. It was next found that plasma, then that serum, even in small amounts (5 or 10 cc.), had the same effect. Finally, a plasma concentrate or extract was prepared as follows:

Plasma was shaken up with two volumes of 95 per cent alcohol and centrifugated. The supernatant fluid was evaporated to dryness in a vacuum at room temperature. The residue was extracted with a small volume of 95 per cent alcohol and filtered. This alcoholic solution was kept until needed. An amount corresponding to 20 cc. of the original blood was then evaporated to dryness, taken up with about 1 cc. of freshly distilled water and used for injection.

In summary, the following conclusion was reached: Because there was reduction in the amount of urobilin excreted, which is interpreted as a reduction in the rate of hemolysis, it seems possible that in these cases one is dealing with an absence of some substance which is present in normal plasma and which in some way prevents excessive hemolysis. This possibility has yet to be tested.

DR. T. B. COOLEY, Detroit: Dr. Josephs is to be congratulated on having taken a rather new approach to this problem. It has seemed to me for some time that both in sickle cell anemia and in hemolytic icterus there must be a lack in the cell-building substances furnished to the marrow. In both these conditions there are cells the structure of which is obviously abnormal. In hemolytic icterus the cell is more globular, with a smaller diameter and a peculiar susceptibility to hemolyzing solutions. The sickle cell has a property of stretching out under the influence of anoxemia and some other conditions, which must depend on some-

thing peculiar in its structure. One would suppose that this might be related to the character of the substances furnished the marrow with which to work.

It would be logical to suppose that the plasma carries building stones to the marrow. One might look for them in the marrow itself. Whipple suggested that in some of these diseases the trouble may lie in the endocrine glands, in which case their secretions may have to be investigated. There is a considerable list of possible factors which might be tested, but the plasma and the marrow are obvious, because normal structural material should be there, no matter where it comes from.

Dr. Josephs used an interesting approach, and I find the change in the excretion of urobilin more interesting than that in the hemoglobin. The resemblance to what happens after transfusion is striking.

DR. S. G. ROSS, Montreal: The work of Dr. Josephs makes one wonder whether, in hemolytic icterus of the new-born, the important factor is not contained in the plasma. If so, it might be advisable to use plasma rather than blood in the treatment of this condition. The possible objection to the use of whole blood is that in hemolytic icterus obstructive jaundice often develops, and the jaundice might be increased by the difficulty of removing the excessive pigment resulting from the destruction of red blood corpuscles. Physicians know that certain of these patients die of obstructive jaundice rather than of the anemia resulting from the hemolysis.

DR. BENJAMIN KRAMER, Brooklyn: Several years ago Hampson reported the recovery of 22 of 23 patients with "familial icterus gravis of the newly born" following the use of intramuscular injections of maternal blood serum. This disease is usually accompanied by severe anemia. We have had occasion to treat an infant, the fifth child. Three previous children had died of icterus gravis. The patient in question was given 50 cc. doses of maternal serum, beginning twenty-four hours after birth, for a total of 200 cc., and although severe jaundice developed, the child, nevertheless, made a complete recovery. The theoretical explanation of this is that maternal serum contains a substance which neutralizes a hemolytic substance in the infant's blood. This explains the fact that the disease develops in utero but early in the neonatal period, presumably because the antihemolytic substance is no longer available.

DR. HUGH W. JOSEPHS, Baltimore: In regard to Dr. Cooley's suggestion that these patients lack something that under normal conditions acts on the marrow, the figures reported here show only a reduction in the excretion of urobilin, which has been interpreted to mean a reduction in the destruction of blood. I failed to point out sufficiently that the percentages for the reticulocytes were not demonstrably affected by the injections. The variations that occurred could be explained on other grounds. This, of course, does not mean that the formation of blood may not be influenced; I have merely been unable as yet to demonstrate any specific influence.

Dr. Marriott asked whether animal blood had been used. I have used only my own blood and some that had been drawn for transfusion but had not been used. One of the next steps is the trial of animal blood, as well as organ extracts, especially bone marrow and liver extracts.

Dr. Kramer has answered Dr. Ross's question regarding icterus of the new-born. The extract has not been used, but maternal plasma is being used extensively in England following Hampson's demonstration of its value in familial cases.

I have yet to see a case of erythroblastic anemia of the type described by Dr. Cooley. Finkelstein, however, reported good results from repeated intramuscular injections of whole blood in cases of von Jaksch's anemia.

EFFECT OF HYPERPYREXIA ON VARIOUS PEDIATRIC CONDITIONS. DR. LOUIS SPEKTER (by invitation) and DR. ANGUS MCBRYDE (by invitation), Durham, N. C.

Patients were placed in a closed cabinet, with only the head outside, and the temperature was raised to from 40 to 41.5 C. (104 to 106.8 F.) by means of the

radiant energy given off by carbon filament lamps. All the 10 children treated were restless and required mild sedatives before the heating began.

Abdominal distention was the most common complication, occurring in about 53 per cent of the treatments. Often this distention was related to the vomiting, but in many cases it was caused by gas in the lower bowel, which could be removed by inserting a rectal tube. Vomiting occurred in about one half of the patients, usually only once, but in a few patients it was prolonged and severe. Early in our series, sodium chloride in tablet form or in 0.6 per cent solution was given, but it definitely increased the vomiting and distention, and so has recently been omitted. Water, fruit juices and broths produced less vomiting and distention. While the blood chlorides were moderately lowered, being perhaps from 50 to 100 mg. per hundred cubic centimeters when no chloride was given, no severe abdominal cramps were noted. The fluid intake varied from 2,500 to 5,000 cc. and the urinary output from 100 to 200 cc. As a rule, the patients maintained or gained weight during heating. The hemoglobin and the red blood cell count were stationary or slightly increased. Only the patients who persistently vomited had marked concentration of blood or loss of weight. In 37 per cent of the treatments the patients complained of abdominal pain, but this usually was not severe and accompanied the distention. Headache was noted during about 20 per cent of the treatments, usually during the latter part. In 18 per cent of the treatments the patient was delirious or could be aroused only with great difficulty. In a child aged 3½ years, the youngest patient treated, generalized convulsions occurred on two occasions about one and one-half and four and one-half hours after the temperature reached 41.3 C. (106.3 F.), but ceased when the temperature was lowered. This child had chronic gonococcic vaginitis, so there was no factor of the so-called toxic action so often postulated in convulsions at the onset of an acute infection. The reactions of any patient during successive fever treatments were likely to be the same.

The 10 children had a total of 29 treatments, and 10 adults had 30 treatments. Several adult males suffering from gonococcic urethritis were treated with temperatures of 41.5 C. (106.8 F.) for five hours. The usual result was a marked decrease in the number of organisms, with the discharge becoming serous and scanty, but forty-eight hours later the discharge and the organisms returned. Only 2 patients with chorea have been treated, both with improvement. This method is more drastic and leaves the patient more prostrated than does the intravenous injection of typhoid vaccine. One child with a Wassermann-fast reaction after two years of treatment with arsenic and bismuth showed no reversal of the Wassermann reaction after two treatments at 40.5 C. (105 F.). Dr. Warren found that 2 patients recovered from brucella infection following fever therapy. One of our patients had had an active brucella infection for two years, despite various therapeutic measures; he was treated with artificial fever at 41 C. (105.8 F.) on four occasions, with some general improvement. His temperature immediately returned to normal or subnormal levels after each treatment, but rose again after a few days. Ten days after the last treatment the condition suddenly became worse, and the patient died within three days, apparently of a secondary infection with a hemolytic staphylococcus. It is possible that in this case fever therapy hastened death.

In each of the 10 adults and 5 children with chronic infectious (atrophic) arthritis treated with artificial fever at 40.5 C. (105 F.) for five hours, two signs of improvement were noted: (1) decrease in, or relief of, pain and (2) increased motion in the joints. This improvement has been maintained over a period of at least several months. In the severe and long-standing cases other measures, especially massage, and passive and active motion were necessary to maintain the ground gained.

The most marked improvement has been in patients with gonococcic arthritis. There was relief of pain in all cases, and if the arthritic process had not caused destruction of bone or ankylosis, motion was almost completely restored after a single treatment. Patients who had been unable to walk for weeks usually could walk the day after the treatment. Massage and active motion were employed

to maintain the improvement, but in several cases it was maintained without these measures.

In presenting this material, we realize that the patients are too few and the time of observation too short to draw any definite conclusions. However, we believe that fever induced by this relatively simple and safe method is of definite value as an additional therapeutic procedure in chronic arthritis. The immediate relief of pain and increase of motion stimulate the patient mentally so that he continues with the prolonged dietary, physiotherapeutic and orthopedic measures which should be used in conjunction with fever therapy.

DR. CHARLES HENDEE SMITH, New York: After hearing in Washington last year about Dr. Warren's box for producing fever, we started to build one at once. We now have two. Our results have been comparable to those of Dr. McBryde. Dr. Sutton and Dr. Dodge have used this method mostly in chorea and have proved to our satisfaction that the results produced with typhoid vaccine are due to fever rather than to any specific protein reaction. The hot box requires fewer treatments, because the temperature can be kept up longer on any given day. The temperature curves obtained are identical with those shown, with a slow rise, a plateau and a gradual fall. The movements may be a little worse after the first day, just as they are after the first fever induced with vaccine, but there is marked improvement within forty-eight hours. We had a patient who was completely cured after being treated twice. Some patients have required a few more treatments.

The trouble with this method is that it is time-consuming and laborious, requiring the constant attention of either a nurse or a physician or both. A technician or a nurse should not have full responsibility, because occasionally sudden spurts of temperature to a dangerous point occur. Two of our patients had convulsions. One of these was a defective child and the other a patient with chorea.

The patients are just about as uncomfortable as when fever is produced with typhoid vaccine. I should prefer to have fever produced by something injected into a vein from which I could not get away rather than fever from a row of lights from which I could get away if some-one would help me. Dr. Sutton and Dr. Dodge do not agree with me, however. They have been using this method in a few cases of early rheumatoid arthritis. If the contention of workers at the Presbyterian Hospital is correct that this disease, as shown by its pathologic changes, is the same as rheumatism, then one is justified in treating it in the same way. The results are equivocal, but a few patients have been helped.

In gonococcic vaginitis the treatment is disappointing, since the temperature must be too high and too long continued to give results.

The hot box is an interesting method of producing fever and is much less expensive and safer than the radiotherm, but it is so time-consuming that in chorea, at least, it does not replace vaccine for routine use.

DR. WILBURT C. DAVISON, Durham, N. C.: No therapy has caused so much improvement in children suffering from chronic arthritis as has this "sweat" box. Invariably, the pain has been relieved, and the motion increased. In regard to the discomfort, children, when asked if they like being in the box, say no, but they are willing to go back the following week because they themselves state that they are helped. The fact that young children follow a procedure that is uncomfortable because they realize its benefit is a great recommendation for this simple form of treatment.

DR. ANGUS MCBRYDE, Durham, N. C.: The child aged 3½ years who had the convulsion had chronic gonococcic vaginitis only. There was no so-called "toxic" factor, which is so often postulated in convulsions at the onset of acute febrile diseases. Mr. Sittler, working with Dr. W. M. Simpson at the Miami Valley Hospital in Dayton, Ohio, has devised a heat cabinet similar in principle to this one, but with circulating air and a lower humidity. The patients are said to be much more comfortable in this more elaborate cabinet, but great comfort is hardly obtainable at such high temperatures.

Sixth Session

Saturady Afternoon, May 5

SALT AND WATER METABOLISM IN A CHILD WITH ADDISON'S DISEASE. DR. H. B. CUSHING, Montreal, Canada.

A boy, 10 years of age, showed the classic symptoms of Addison's disease. Death came during an attack of extreme hypoglycemia, and autopsy showed congenital absence of one suprarenal gland and marked hypoplasia and atrophy of the other. The blood during life showed concentration due to dehydration, and a tendency to low sodium, chloride and sugar contents. The administration of sodium chloride in capsules, in doses of 8 to 10 Gm. per day, was required to maintain a normal water, sodium and chloride balance.

Observation of this and similar cases and recently published observations on suprarenalectomized dogs and cats indicated (1) that one of the main functions of the suprarenal cortex is to maintain the sodium chloride balance of the organism and, through this, the water balance and (2) that the loss of these balances leads to a definite clinical syndrome consisting of dehydration, hemoconcentration, circulatory collapse and sudden death (this syndrome being quickly relieved either by the use of cortin or by the administration of sodium chloride).

It is suggested that a similar syndrome in the course of other diseases of childhood may be due to impaired function of the suprarenal cortex.

DISCUSSION

DR. DANIEL C. DARROW, New Haven, Conn.: I should like to ask Dr. Cushing what the findings were when the patient went into collapse and had a negative sodium chloride balance.

DR. FRANK C. NEFF, Kansas City, Mo.: Do you have records in your hospital of any previous cases?

DR. H. B. CUSHING, Montreal, Canada: In regard to loss of weight, it is not easy to make a statement offhand, because the patient lost different amounts at different times. On admission, the weight was 42 pounds (19.1 Kg.), and the patient weighed 46 pounds (20.9 Kg.) within two or three days. His weight gradually increased until it reached 50 pounds (22.7 Kg.). On different occasions he lost from 2 to 4 pounds (0.9 to 1.8 Kg.) with a negative sodium chloride balance and rapidly regained that on the administration of salt.

As to the number of such patients with Addison's disease admitted to the hospital, I do not remember another case of typical Addison's disease in a child. Two or 3 children were admitted to the hospital who died suddenly of some unknown cause and after death were observed to have destruction of the suprarenal glands, but the diagnosis was not made during life.

CHRONIC HYPOGLYCEMIA IN CHILDHOOD. DR. BENJAMIN KRAMER, DR. H. G. GRAYZEL (by invitation) and DR. CHARLES I. SOLOMON (by invitation), Brooklyn.

Two cases of chronic persistent hypoglycemia in young children are presented. In one, the causative factor was extensive fatty infiltration of the liver which resulted in interference with the hepatic functions of glycogenesis and glycogenolysis. In the second, hyperinsulinism was probably responsible for the hypoglycemia and its attendant symptoms. However, the pathologic condition responsible for the hyperinsulinism has not yet been definitely determined. Although a pancreatic condition, such as an adenoma or hypertrophy and hyperplasia of the islands of Langerhans, was the most probable cause, in view of the neurologic condition present in this child one must entertain the possibility that the hypoglycemia was neurogenic.

DISCUSSION

DR. SAMUEL AMBERG, Rochester, Minn.: We had an infant 10 months old, who belonged, perhaps, to the same group. Perhaps the first case of this type was described by Wagner and Parnass, who on the use of the epinephrine test did not get mobilization of sugar. Our case of hypoglycemia in an infant with an enormous liver is interesting from several points of view. The acetone bodies in the urine were low. On the administration of 0.25 mg. of epinephrine no mobilization of sugar occurred; with 0.5 mg., the blood sugar rose from 56 to about 110 mg. In agreement with the studies of von Creveland, there was an increased cholesterol level of 238 mg. There was moderate retention of nitrogen. Our study of the case was interrupted, unfortunately, by an attack of hepatitis or hepatoptosis, with jaundice, the stools containing bile.

The group that Dr. Kramer described is extremely interesting. I dare say that the number of cases will increase and that one will have to distinguish several subgroups.

DR. ALEXIS F. HARTMANN, St. Louis: Dr. Kramer properly emphasized the fact that there are a number of reasons for the development of hypoglycemia. Our experience at the St. Louis Children's Hospital has been exceptionally rich in confirming that impression. I have in mind 5 patients showing four different causes for hypoglycemia. Two were babies born of diabetic mothers. In 1, symptoms of hypoglycemia and convulsions began twenty-four hours after birth; in the other, six hours after birth. The treatment was relatively simple, requiring merely dextrose given parenterally for the first four or five days, after which the babies behaved normally.

An interesting point was noted when carbohydrate was given by gavage, with the idea of getting more sugar into these infants. Such gavage was followed by projectile vomiting. Under the fluoroscope obvious pylorospasm was present, similar to that in pyloric stenosis. When the blood sugar was brought to normal and maintained at normal, the pylorospasm ceased, and the infants could be fed sugar by mouth.

Of the remaining 3 cases, 1 is interesting but is not so important. The patient was accustomed to raiding the icebox and getting all the jam and jelly that he could eat; he was caught, not red-handed, but literally red-faced with jam. A padlock was placed on the icebox, and shortly afterward he went into hypoglycemic shock. He was allowed to get back into the icebox at reasonable intervals.

In the remaining 2 cases we had considerable trouble. One is particularly interesting. A year ago, a 1 year old baby was brought to the hospital with the history of having had convulsions since about the age of 3 months. When admitted, she was fat, flabby and hypotonic, could not sit alone and looked mentally deficient. She had convulsions on the day of admission; the blood sugar was 20 mg. per one hundred cubic centimeters during the preliminary period of study and it remained at that level or lower. Sugar could be mobilized from the liver by the administration of epinephrine. A respiratory infection developed while she was in the hospital. She became slightly diabetic for several days, and the sugar returned to the low level. Pituitary extracts failed to raise the blood sugar. At operation the liver looked normal grossly and, later, in sections. The pancreas looked normal also, and as much as about seven eighths of the entire gland was removed. This excised portion was later subjected to study, and was observed to be normal. The operation was performed last July. The child was brought back for examination a month ago; the blood sugar level was normal; the sugar tolerance test gave normal results, and mental development since that time was what one would have expected over that period. She was still mentally a half year behind her age.

The last case, which is even more interesting, is that of a boy who has periodic attacks of severe hypoglycemic symptoms, in which convulsions develop. The patient has been brought to the hospital in a coma about every six months for the last three years. He has been in the hospital for a number of months since his last admission. The blood sugar during fasting has been determined daily,

altogether about a hundred and fifty times. The determinations show waves dipping occasionally to as low as about 50 mg. per hundred cubic centimeters and then going back to about 70 or 80 mg. (true dextrose). If he is given 2 units of insulin, the blood sugar drops from the normal level to about 18 mg. or so, and he collapses. He can be brought out promptly by the administration of epinephrine or the intravenous injection of dextrose. This case represents a type of hypersensitivity to insulin which may be caused by suprarenal dysfunction.

DR. HUGH W. JOSEPHS, Baltimore: I was interested in the failure to react to epinephrine manifested by this patient. Absence of the usual hyperglycemia following the injection of epinephrine has been emphasized as one of the principal points in the diagnosis of von Gierke's disease. In a case that Dr. Ross and I reported there was an interesting variation in the reaction to epinephrine. The child was one who had recurrent acute attacks of hypoglycemia, which could be initiated by short periods of fasting. During one of his attacks, when the blood sugar was 45 mg. per hundred cubic centimeters, we failed to obtain any rise in the blood sugar following the injection of epinephrine, whereas later, when the blood sugar was normal, the response to epinephrine was normal.

DR. BÉLA SCHICK, New York: The April issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN contains an observation from my department concerning a case of von Gierke's disease characterized by enlargement of the liver, hypoglycemia and acetone in the urine.

Several years ago I saw the famous case of Wagner and Parnass, the first one belonging in that group. Real diabetes developed in that child. The blood sugar level was about zero. It was interesting that in spite of the high acetonemia she did not show any symptoms of cyclic vomiting. The child felt relatively well.

There are cases described in the literature in which idiopathic hypertrophy of the heart was due to an accumulation of glycogen in the muscle cells. Patients with pyloric stenosis should also be examined for glycogen.

DR. L. EMMETT HOLT JR., Baltimore: Dr. Kramer made the suggestion that the accumulation of fat in the liver was due to the formation of fat from carbohydrate. It seems equally possible that the fat accumulated because of some primary difficulty in the liver. The fat which was mobilized from the depots into the blood was not burned or utilized when it reached the liver. It would have been possible to test this by following the rate of disappearance from the blood of fat injected intravenously.

DR. BENJAMIN KRAMER, Brooklyn: In regard to Dr. Higgins' suggestion, we have not attempted to interpret the levulose curve because we were unable to obtain a quantitative collection of urine. All we know is that there was no increase in the reducing substance in the blood after the administration of levulose.

I am sorry that I did not make myself clear to Dr. Amberg. I attempted to emphasize the points of difference between this case and the type of disease described by von Gierke.

There are, no doubt, a number of clinical conditions associated with hypoglycemia. Dr. Cushing mentioned lack of development of the suprarenal cortex. Of course, hypoglycemia may be part of the syndrome of Addison's disease. We have another case which I did not report, but which will be reported in the article on hypoglycemia when it is published. The second patient had definite neurologic changes. Vomiting was not a striking symptom in this case. The child took a mixed diet and retained it, for the most part. Although we have shown a single epinephrine curve, we did several on this patient; the result was always the same.

EFFECT OF CHANGES IN EXTRACELLULAR ELECTROLYTE ON CELLULAR ELECTROLYTE AND WATER. DR. DANIEL C. DARROW and DR. HERMAN YANNET (by invitation), New Haven, Conn.

Dogs, monkeys and rabbits were used. An intraperitoneal injection of a solution of 5 per cent dextrose was performed on each. After about five hours the amount of fluid in the peritoneum was about the same as that injected, but it then

contained electrolyte approximately of the composition of that in extracellular fluid. Since the fluid in the peritoneum may be regarded as temporarily outside the body, the content of body water was unchanged, but the available electrolyte of extracellular fluid was reduced by the amount of sodium, chloride, bicarbonate, etc., diffusing into the peritoneum.

The reduction of extracellular electrolyte brought about shifts of body water so as to bring the osmotic pressure of cellular and extracellular fluid into equilibrium. Although the experimental animals had the normal quantity of water in the body, most of the signs and symptoms of clinical dehydration developed. Study of the protein and electrolyte content of the serum and red cells revealed that the serum protein and erythrocytes were increased, but that the concentrations of electrolyte of both the serum and the erythrocytes were reduced. The reduction of serum electrolyte was brought about by a shift of extracellular electrolyte into the peritoneum without an accompanying shift of water. The decrease in erythrocytic concentration of electrolyte was the result of a shift of water from extracellular spaces into the red cells. Presumably, the clinical appearance of dehydration was due to the fact that all the cells of the body behaved as the erythrocytes, and a shift of water from extracellular spaces into the cells took place, which reduced the volume of extracellular fluid considerably.

Similar experiments were performed, using 1.8 per cent sodium chloride. This procedure increased extracellular electrocyte without altering body water. Clinically, the animals showed few symptoms besides thirst. The serum protein and erythrocytes were reduced. However, the concentrations of electrolyte of both the cells and the serum were increased. The concentration of electrolyte in extracellular spaces was brought about by the absorption of sodium chloride without water, and the concentration of cellular electrolyte was brought about by a shift of water from the cells to extracellular spaces.

It is pointed out that the first type of experiment may be closely analogous to what takes place in acute suprarenal insufficiency and certain phases of diarrheal disease when the patients are treated with water alone. The second type of experiment may be simulated when loss of water by insensible perspiration is not replaced.

DISCUSSION

DR. ALEXIS F. HARTMANN, St. Louis: In connection with some of the data that Dr. Darrow cited, I can think of at least one application. It has been the habit of the neurosurgeons, when they perform operations for the surgical relief of hydrocephalus, to allow spinal fluid to escape from the ventricles and then to refill them with physiologic solution of sodium chloride.

Following such procedures my associates and I have frequently noted the appearance of shock, with chemical changes in the blood, which included lowering of bicarbonate. It occurred to us that the real reason for the occurrence of shock was that the spinal fluid lost sometimes amounted to more than the circulating volume of blood when the hydrocephalus was marked. We thought that possibly we could prevent such symptoms of shock if we replaced the fluid removed with fluid similar in composition. We made such a fluid in two halves; one half was sodium carbonate and the other half was a mixture of salts containing sodium, potassium, calcium and magnesium chlorides. Hydrochloric acid in the proper amount was added to the solution of sodium carbonate to convert it into sodium bicarbonate and sodium chloride, and then the two halves were mixed in equal volumes. The resulting mixture was similar to normal cerebrospinal fluid in regard to sodium, potassium, calcium, magnesium, chloride, bicarbonate and p_H. Following the use of such a solution the infants seemed to withstand the effect of the operation much better.

DR. A. A. WEECH, New York: I should like to inquire whether Dr. Darrow has observed similar changes in the distribution of electrolytes and water in the blood following the rectal administration of solutions of dextrose.

DR. DANIEL C. DARROW, New Haven, Conn.: In answer to the question regarding the bearing of these experiments on the parenteral use of dextrose, I

think, in the first place, that 10 per cent of the body weight is somewhat more solution of dextrose than may be given subcutaneously or intraperitoneally, even in our most ambitious moods, but it is not a great deal beyond that amount. So in this sense the experiments may show the type of changes that the subcutaneous injection of dextrose may produce. In regard to whether a solution of dextrose produces the same changes when injected into the intestines, similar results were obtained in rabbits in which the fluid was accidentally introduced into the colon instead of into the peritoneum.

Schechter's experiments revealing the changes in composition of fluids injected into the peritoneal cavity were the outgrowth of my belief that a solution of dextrose placed in subcutaneous tissues or in the peritoneal cavity is irritating. I believed that so-called isotonic dextrose is not in equilibrium with tissues. I imagine that every one of the members has seen 5 per cent dextrose injected subcutaneously, with no grave consequence. However, any one who has seen it used extensively has observed that subsequent absorption was slow and that occasionally the site of injection remained boggy and sore for several days. In subcutaneous tissues it would be difficult to demonstrate that the amount of fluid increased during the first hours after the injection. I am sure that this occurs. However, with the larger amounts of fluid injected into the peritoneal cavity, I am sure that under certain circumstances, when the patient is already dehydrated, sufficient fluid may be withdrawn from the body temporarily to aggravate the dehydration.

Our rule at the New Haven Hospital is that 5 per cent solution of dextrose shall never be given subcutaneously or intraperitoneally. When it seems desirable to give a solution containing less electrolyte than physiologic solution of sodium chloride, a mixture of equal parts of 5 per cent dextrose and physiologic solution of sodium chloride may be given. Such a solution has no dehydrating effect, is not irritating locally and provides a solution containing less electrolyte than physiologic solution of sodium chloride. However, such a solution does not provide much dextrose; therefore, if one wants to give much dextrose parenterally, intravenous infusions must be used.

METHODS FOR THE RELIEF OF DIABETIC ACIDOSIS. DR. ALEXIS F. HARTMANN, St. Louis.

The method of treating severe diabetic intoxication which is used at present in the St. Louis Children's Hospital is recommended for the following reasons: (1) It provides a very rapid yet safe method of restoring the normal acid-base balance of the blood in its broadest sense; (2) it leads to rapid abolition of ketosis, hyperglycemia and glycosuria, and (3) it can be carried out as a simple, standardized procedure requiring usually but from thirty to forty-five minutes for completion, with little or no assistance from the laboratory (with the possible exception of data occasionally necessary for establishing with certainty the diagnosis of diabetic acidosis).

As soon as the diagnosis of severe or extreme diabetic acidosis is made, insulin in a dose of approximately 2 units per kilogram of body weight is administered, one-half being given intravenously and one-half subcutaneously. Approximately 10 cc. of molar racemic sodium lactate per kilogram of body weight is then added to 5 volumes of sterile distilled water, and the resulting isotonic mixture (one-sixth molar) is then administered as rapidly as possible. Usually, about one-half is given intravenously, during the administration of which the remainder is given subcutaneously and intraperitoneally. As soon as the isotonic lactate solution has been absorbed from the peritoneal cavity or subcutaneous tissue, slightly hypotonic Ringer's solution is given subcutaneously and intraperitoneally in an amount sufficient to relieve completely any remaining dehydration. This usually amounts to about 40 cc. per kilogram of body weight and generally can be given in a single injection. The total amount of fluid thus given is about 100 cc. per kilogram of body weight, which represents the average loss of weight suffered by the diabetic patient during the development of severe acidosis. The time required to administer

the insulin, lactate and Ringer's solution is usually from one-half to one hour. Absorption is largely completed within an hour or two after the injection. By this time the tendency to vomit is usually much less, and the patient is encouraged to take water by mouth, if he is sufficiently conscious to swallow and if he can retain it. Six hours after the initial injection of insulin the injection is repeated subcutaneously, using a dose of one-half unit per kilogram of body weight. Further, the injections of insulin are given at six hour intervals, the dose being regulated by the blood sugar determination or by examination of the urine, until the patient can be relied on to take his regular meals, at which time the administration of insulin can gradually be adjusted to meet the patient's particular requirements.

The results by this method are compared with those obtained without the use of alkali and those with the use of sodium bicarbonate in place of sodium lactate. As compared with the therapy without the use of alkali, the method has the particular advantage of causing much more rapid recovery from acidosis. The substitution of sodium lactate for sodium bicarbonate adds to both the safety and the simplicity of administration.

DISCUSSION

DR. L. EMMETT HOLT JR., Baltimore: Dr. Hartmann has given a convincing demonstration of the value of alkali treatment, but the difference between the curves of recovery with bicarbonate and with lactate therapy needs further elucidation. If I read the figures correctly, the dose of lactate was more than twice as large as the dose of bicarbonate. I wonder whether the curve for carbon dioxide with bicarbonate therapy would not have risen as rapidly as the curve with lactate, if the dose had been the same. Also the shape of the two curves, I think, requires an explanation; I wonder whether Dr. Hartmann has an explanation for that.

DR. DANIEL C. DARROW, New Haven, Conn.: I was particularly pleased when Dr. Hartmann pointed out that the rapidity of recovery from diabetic acidosis is related chiefly to the period of time it takes the patients to go into coma. Since most of our patients go into coma in a period from eight to twelve hours, recovery takes place within an equally short time. Our diabetic patients are almost entirely trained ones who do not permit themselves to get into the worst condition.

I wonder about the advisability of stressing the use of sodium lactate or sodium bicarbonate before the use of sodium chloride. In a patient with diabetic coma the primary factor to be treated is deficit of extracellular electrolyte. If one supplied sodium lactate or sodium bicarbonate without at the same time supplying sodium chloride, I should think that one was not doing as well as if one gave both simultaneously. I realize that this is largely an academic theory and that statistically no difference between the two methods can be proved.

DR. ALEXIS F. HARTMANN, St. Louis: Dr. Holt's questions are natural, and I think that I can answer them to his satisfaction. The total amount of alkali given as sodium lactate was slightly more than double that given as sodium bicarbonate. The reason we gave the amount of sodium bicarbonate which we did was because we thought that this was the largest dose which we could give safely. The principal reason for changing from bicarbonate to lactate was to assure safety.

It is easy to precipitate a patient from a zone of uncompensated acidosis into a zone of uncompensated alkalosis if one gives sodium bicarbonate in an amount equal to that lost from the body and if one supplies it rapidly, without allowing time for carbon dioxide to accumulate.

Since it takes several hours for lactate to be converted into bicarbonate, we believed that we could give much more than the equivalent of 0.5 Gm. of bicarbonate per kilogram of body weight, and sometimes we gave four times that amount. In the previous work we took the initial carbon dioxide content of the serum, calculated the amount of alkali that had been lost on the basis of body weight and then gave that amount of sodium lactate, getting rather good agreement between the actual and the expected increases in carbon dioxide content.

This may answer the question about the speed of the recovery with the two alkalis. So far as the shape of the curves is concerned, I do not think that the shape of the bicarbonate curve is significant. There were only 8 cases. In 2

the curve rose slowly because of the poor initial circulation and then rose rapidly within from four to six hours. I believe that if we had had a larger group of cases not showing such circulatory disturbance, we should have had a curve rising more rapidly and tapering off.

Had we examined the blood during the first hour of treatment, we probably should have noted a rapid rise to a small extent followed by slowing up and then acceleration. With lactate, one would expect a slower rise during the first hour.

Dr. Darrow's point brings up a fundamental question. I disagree with him that the most important measure in the treatment of diabetic patients with severe acidosis is to resupply basic chloride. In the first place, the amount of chloride that is lost is usually not great. In my mind, the important thing is the extreme acidosis associated with the fall in p_H to such values as 6.95, which we obtained in one instance, and 7, which we obtained in another, which results from the reduction of bicarbonate.

I think that the most important measure is to restore the p_H and bicarbonate value to somewhere within normal limits. In our method of treatment the value of the administration of chloride lies not in the relief of acidosis as the result of excretion of ammonium chloride into the urine, but in the reestablishment of a normal chloride level which permits a normal total concentration of base to be maintained without excess of the bicarbonate ion. In other words, we give Ringer's solution to prevent alkalosis.

We use racemic lactate. There is a difference in the behavior of the two isomers. What used to be called dextrorotatory lactic acid (now called *l*+-lactic acid) is metabolized more rapidly and completely, being apparently entirely converted into glycogen within two or three hours. The other isomer, *d*-lactic acid, is largely oxidized; some escapes into the urine—as much as 5 per cent in such dehydrated patients as these and as much as 30 per cent of the total given to normal persons, who begin to urinate immediately after the administration of such amounts of lactic acid.

One more important point, which I forgot to mention, is why I think one of the patients who received a large dose of sodium lactate died. I mentioned that the temperature rose to 42.5 C. (108.5 F.) and that I thought that we were responsible. This patient was given the lactate in molar concentration and in an extremely large dose—18.5 cc. of molar solution per kilogram of body weight. It is all right to give animals or normal persons such a concentration of lactate. They can drink and easily make up for water needs, but this patient was dehydrated, and even though we followed the intravenous injection of this hypertonic lactate with Ringer's solution, hyperpyrexia developed. In normal subjects, after the administration of considerably smaller amounts of lactate the consumption of oxygen rises about 30 per cent, so that there is increased oxidation, which gives more heat; such an increase in heat may not be dissipated in a dehydrated patient. That was early in our experience, and we shall not make such a mistake again.

Book Reviews

Pediatric Nursing. By Gladys Sellew, M.A., B.S., R.N. Third edition. Cloth. Price, $2.50. Pp. 609, with 53 illustrations. Philadelphia: W. B. Saunders Company, 1934.

The third edition of "Pediatric Nursing," by Miss Gladys Sellew, was published in January of this year by the W. B. Saunders Company.

Miss Sellew is a graduate of the School of Nursing and Health, University of Cincinnati. She has been assistant dean of Cook County School of Nursing; assistant professor in Nursing Education in the School of Nursing, Western Reserve University, and director of nursing service in the Babies and Childrens Hospital, Cleveland and is now director of nursing education in the Chicago City Infant Hospital, which is affiliated with De Paul University. With her training and experience, Miss Sellew is exceptionally qualified to write this complete and authoritative textbook. The first edition of "Pediatric Nursing" appeared in 1926; it was revised, reset, reprinted and recopyrighted in 1930, and has again been completely revised and reset.

Miss Sellew realized that only three or four months of the student's training are given to the study of pediatric nursing and that a complete textbook for further study and reference is necessary for the skilled nurse; hence she prepared this simple, clear and thorough presentation of the subject. She is especially anxious that the nurse should understand both well and ill children.

In the introduction, she has graciously acknowledged the assistance and help which she received in hospitals from different physicians, instructors and nurses, and from the *American Journal of Nursing,* and in so doing convinces the reader of her excellent preparedness for her work.

The book contains six hundred and nine pages and is divided into two parts. Part 1 is divided into seven chapters devoted to the practical discussion of the expectant mother and the care of the normal child, the new-born child, the infant and the growing child. Part 2 contains nineteen chapters and treats of nursing procedures. Each chapter presents one subject (with its subdivisions) and is complete in itself. Throughout the book the author has emphasized all the new developments in pediatric nursing and diseases of children.

There are several unusually helpful and outstanding features of the book: The subject matter is treated in the proper sequence; at the close of each chapter there is a list of suggestive questions on the material of that chapter, and at the end of many chapters there are excellent outlines, which are always of great assistance in mastering a subject. In certain chapters are given the steps in the order in which certain work or preparation for certain work should be done. Diets for children of different ages are given. There are also included lists of books of reference, a list of books for children 5 years old and over and a splendid bibliography of child guidance and books for young children. The index is especially clear and comprehensive.

Any one who is especially interested in pediatric nursing will recognize Miss Sellew's textbook as an unusually scholarly presentation and will recommend it as a textbook for student nurses and as a book of reference for graduate nurses.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: R. C. Jewesbury, Esq., M.D., 5 Wimpole St., W. 1, London.
Secretary: Dr. Helen Mackay, 28 John St., W. C. 1, London.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. A. Graeme Mitchell, Children's Hospital, Cincinnati.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Atlantic City, N. J. Time: June 10-14, 1935.

American Academy of Pediatrics

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: New York. Time: June 7-8, 1935.
Region I. Place: New York, Ambassador Hotel. Time: Oct. 19-20, 1934.
Region II. Place: San Antonio, Texas. Time: Nov. 14, 1934.
Region III. Place: Cincinnati. Time: Fall, 1935.
Time: Oct. 5-6, 1934.
Region IV. Place: Oakland, Calif. Time: November 1934.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

American Pediatric Society

President: Dr. Borden S. Veeder, 3720 Washington Ave., St. Louis.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Wade Park Manor, Cleveland. Time: May 2-4, 1935.

Canadian Society for the Study of Diseases of Children

President: Dr. D. P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.
Place: Buffalo, N. Y. Time: June 1935.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Society of Pediatric Research

President: Dr. Joseph Stokes Jr., Children's Hospital, Philadelphia.
Secretary: Dr. A. A. Weech, Babies Hospital, New York.
Place: Atlantic City, N. J. Time: May 1935.

SECTIONAL

North Pacific Pediatric Society

President: Dr. Armin Rembe, Stimson Bldg., Seattle.
Secretary: Dr. Frank H. Douglass, 1227 Medical and Dental Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Oliver W. Hill, 301 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.
Place: San Antonio, Texas. Time: Nov. 13-16, 1934.

STATE

Alabama Pediatric Society

President: Dr. Charles Abbott, 1817 Broad St., Tusaloosa.
Secretary-Treasurer: Dr. Wallace Clyde, Employee's Hospital, Fairfield.
Place: Mobile. Time: April 17-19, 1935.

Georgia Pediatric Society

President: Dr. Benjamin Bashinski, 700 Spring St., Macon.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta. Time: Dec. 13, 1934.

Louisiana State Pediatric Society

President: Dr. John Signorelli, 2000 Tulane Ave., New Orleans.
Secretary-Treasurer: Dr. Edwin A. Socola, 1027 Canal Bank Bldg., New Orleans.
Place: New Orleans. Time: April 29, 1935.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Place: Flint. Time: September 1935.

Mississippi State Pediatric Society

President: Dr. N. C. Womack, Jackson Infirmary, Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 725 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. Fifth St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. Seventh St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. C. V. Rice, 222 Wall St., Muskogee.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.
Place: Oklahoma City. Time: May 1935.

South Carolina Pediatric Society

President: Dr. Julian P. Price, Medical Bldg., Florence.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.
Place: Columbia. Time: January 1935.

Tennessee State Pediatric Society

President: Dr. Arthur G. Jacobs, 1193 Madison Ave., Memphis.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Place: Nashville. Time: April 1935.

Texas Pediatric Society

President: Dr. Ramsay H. Moore, 3600 Fairmount St., Dallas.
Secretary-Treasurer: Dr. F. H. Lancaster, Medical Arts Bldg., Houston.
Place: San Antonio. Time: Nov. 13, 1934.

Virginia Pediatric Society

President: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry M. Greenwald, 499 Ocean Ave., Brooklyn.
Secretary: Dr. Sylvan D. Lazarus, 847 Lincoln Place, Brooklyn.
Place: Medical Society of County of Kings Bldg., 1313 Bedford Ave., Brooklyn.
Time: Third Wednesday of each month from October to May, 8:30 p. m.

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg., Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Morris Gleich, 9 Post Ave., New York.
Secretary: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Stanley Gibson, 9503 Prospect Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: John B. Murphy Memorial Bldg. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Earl W. May, 1551 Woodward Ave., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Muse, 384 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Frank Lancaster, Medical Arts Bldg., Houston, Texas.
Secretary-Treasurer: Dr. A. A. Little Jr., 817 Holman Ave., Houston, Texas.
Place: Houston Club: Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Henry A. Reisman, 148, 88th Ave., Jamaica, L. I.
Secretary-Treasurer: Dr. Edith A. Mittell, 112 Queens Blvd., Forest Hills, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

Milwaukee Pediatric Society

President: Dr. F. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Secretary: Dr. John H. Reynolds, 1628 Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. James L. Gamble, 300 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Harry Bakwin, 132 E. 71st St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. O. W. Rowe, 205 W. 2nd St., Duluth, Minn.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S. Minneapolis.
Place: Minneapolis. Time: Spring, 1935.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Henry C. Flood, Highland Bldg., Pittsburgh.
Secretary: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. W. A. McGee, 616 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Secretary: Dr. Ralph Verploeg, 19th and Gilpin Sts., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Armin C. Rembe, Stimson Bldg., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. John F. Sanders. 320 Townsend St., Lansing, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Nov. 23-24, 1934.